This is a digital copy of a book that was preserved for generations on library shelves before it was carefully scanned by Google as part of a project to make the world's books discoverable online.

It has survived long enough for the copyright to expire and the book to enter the public domain. A public domain book is one that was never subject to copyright or whose legal copyright term has expired. Whether a book is in the public domain may vary country to country. Public domain books are our gateways to the past, representing a wealth of history, culture and knowledge that's often difficult to discover.

Marks, notations and other marginalia present in the original volume will appear in this file - a reminder of this book's long journey from the publisher to a library and finally to you.

Usage guidelines

Google is proud to partner with libraries to digitize public domain materials and make them widely accessible. Public domain books belong to the public and we are merely their custodians. Nevertheless, this work is expensive, so in order to keep providing this resource, we have taken steps to prevent abuse by commercial parties, including placing technical restrictions on automated querying.

We also ask that you:

+ *Make non-commercial use of the files* We designed Google Book Search for use by individuals, and we request that you use these files for personal, non-commercial purposes.

+ *Refrain from automated querying* Do not send automated queries of any sort to Google's system: If you are conducting research on machine translation, optical character recognition or other areas where access to a large amount of text is helpful, please contact us. We encourage the use of public domain materials for these purposes and may be able to help.

+ *Maintain attribution* The Google "watermark" you see on each file is essential for informing people about this project and helping them find additional materials through Google Book Search. Please do not remove it.

+ *Keep it legal* Whatever your use, remember that you are responsible for ensuring that what you are doing is legal. Do not assume that just because we believe a book is in the public domain for users in the United States, that the work is also in the public domain for users in other countries. Whether a book is still in copyright varies from country to country, and we can't offer guidance on whether any specific use of any specific book is allowed. Please do not assume that a book's appearance in Google Book Search means it can be used in any manner anywhere in the world. Copyright infringement liability can be quite severe.

About Google Book Search

Google's mission is to organize the world's information and to make it universally accessible and useful. Google Book Search helps readers discover the world's books while helping authors and publishers reach new audiences. You can search through the full text of this book on the web at `http://books.google.com/`

LANE
MEDICAL LIBRARY
Exchange
Harvard Medical School

HUMAN PHYSIOLOGY

PRINTED BY
SPOTTISWOODE AND CO., NEW-STREET SQUARE
LONDON

AN INTRODUCTION

TO

HUMAN PHYSIOLOGY

BY

AUGUSTUS D. WALLER, M.D.

LECTURER ON PHYSIOLOGY AT ST MARY'S HOSPITAL MEDICAL SCHOOL, LONDON
LATE EXTERNAL EXAMINER AT THE VICTORIA UNIVERSITY

LONDON
LONGMANS, GREEN, AND CO.
AND NEW YORK: 15 EAST 16th STREET
1891

All rights reserved

F34.
W19
1891

TO THE MEMORY
OF
MY FATHER

AUGUSTUS WALLER, M.D., F.R.S.

1816—1870

Emigration of Leucocytes, 1846
Degeneration and Regeneration of Nerve, 1850
Cilio-spinal Region, 1851
Vaso-constrictor Action of Sympathetic, 1853

PREFACE

I HAVE WRITTEN this book with a distinct consciousness that physiology in a medical school is, in conjunction with anatomy, the introduction to medicine and to surgery of those who will be engaged in 'general practice,' and I hope that the volume may be found to justify its title of 'Human Physiology' with reference to the position which the subject should occupy in medical education, as the junction to which anatomy, chemistry, and physics converge, and from which the principles of medicine and of surgery diverge.

Physiology does not consist in a knowledge of recondite phenomena, of difficult names, and of complicated instruments. It should fundamentally consist in the living mental picture of what the great organs below a man's skin are like, what they are doing, how they can be examined, what happens when they are not working properly, how their actions hang together, how they may be influenced for good and for evil. But physiology, as it is written, contains more than this, and, in sparing measure, it is well that the 'Institutes of Medicine' should not be restricted to the visibly 'useful,' or to the obviously 'utilisable.'

A short course of practical physiology is of the utmost value to the student of medicine, not merely because it puts into his hands the methods of everyday

77802

medical chemistry and physics, but because it helps to correct that credulous bias or primitive 'suggestibility' which is a physiological property of the human brain, and only too apt to be fostered by unmitigated book-work. *Practical* physiology is the indispensable adjuvant and corrective of book-physiology, because it brings words to the touchstone of physical instruments and of chemical tests, because the conversion of phrases into facts gives measure of their relative value, and is at the same time an exercise of patience and of judgment—in short, because it is a rational discipline, as well as a useful technique.

Nor is this all. An acquaintance with at least the existence of frontier interests, and even a participation *de tactu* with the science at its growing surface, cannot be excluded from the laboratories of a medical school without serious and immediate loss to the interests of medicine and of surgery.

With regard to the plan of construction of this book. The chapter headings are intended to serve a double purpose; as a summary or syllabus—being, in fact, the condensed lecture-syllabus which I have used during the last seven years—and as a means of self-examination. A student having read certain paragraphs or chapters should return to the chapter headings, and find by their recapitulation whether they contain expressions which are meaningless to him, or whether they recall a series of ideas which he has understood and assimilated.

Certain subjects are more difficult than others: som are more suitably studied during the first year, other during the second year; others, again, are difficult and c practical importance, some are difficult and of scientifi importance. One subject may deserve days or weeks study, and require thorough analytic treatment, or b adapted to experimental demonstration; others may be more lightly passed over. Detailed guidance in such matters will be supplied by the discretion of the teacher, and by the traditions current among examinees; but, in order to give some general guidance to the private reader, occasional use has been made of an asterisk in the chapter headings. In Part I. the sign has been freely used to indicate portions upon which a first-year student should not spend time if he should find the subject difficult. In Part II. the sign has been sparingly used, to indicate portions of undoubted difficulty, which can be omitted by a second-year student who is not reading for the higher examinations. Subjects of unmistakeable difficulty in Part II., such as 'the brain,' 'vision,' &c., have not been so marked, because their great practical importance demands early and patient study from every student of medicine.

The descriptions of figures are to be regarded as forming part of the text, inasmuch as they frequently contain statements of fact which are not included in the text. The Appendix contains matter which was felt to interfere with continuity of description in the main account of physiological phenomena.

I have given a Bibliography after some hesitation, feeling that references to original papers are of no use to junior students, and must be too imperfect to be satisfactory to more advanced students. But to do so has allowed the text to be lightened of names, while preserving for the student who may inquire further, the authorities for the principal statements made. Moreover, the chief use of a bibliography in a general text-book is to afford a few main starting-points and indications, to be followed up in the year-books and archives of a well-equipped library, and even for junior students, it ought to be of some assistance to know whether doctrines and statements date from last year or from last century; the year of publication has been given in each case, leaving the particular page of a particular paper to be looked up in the index of the journal to which reference has been made.

I have, in conclusion, to express my thanks for the friendly criticism and suggestions which have been afforded me by Dr. Mott during the revision of proof-sheets.

CONTENTS

PART I

THE PHENOMENA OF NUTRITION

CHAPTER PAGE
I. INTRODUCTION 1
II. THE BLOOD 8
III. CIRCULATION 41
IV. RESPIRATION 115
V. DIGESTION 155
VI. RENAL EXCRETION 222
VII. FOOD, NUTRITION AND EXCRETION. ANIMAL HEAT . 248

PART II

THE PHENOMENA OF EXCITATION

VIII. GENERAL PLAN OF THE NERVOUS SYSTEM 290
IX. THE PERIPHERAL NERVOUS SYSTEM. MUSCLE . . 301
X. THE PERIPHERAL NERVOUS SYSTEM. NERVE . . . 344
XI. ANIMAL ELECTRICITY 379
XII. LIGHT AND VISION 395
XIII. SOUND AND HEARING. OTHER SENSES 452
XIV. THE SPINAL CORD AND BULB 468
XV. THE BRAIN 502

APPENDIX

I. ORIGIN AND NUTRITION OF THE EMBRYO 557
II. CONSTITUTIONAL FORMULÆ OF PROXIMATE PRINCIPLES . 570
III. UNITS OF MEASUREMENT 577

BIBLIOGRAPHY 581

INDEX 597

Errata

P. 11, line 18 [wrongly given in Addenda, p. 580, as line 8], *for* μ *read* 2 μ.
P. 100, end of first paragraph, *for* p. 104 *read* p. 105.
P. 506, first cut of fig. 264, *letters* L and R should be transposed.

PHYSIOLOGY

PART I

THE PHENOMENA OF NUTRITION

CHAPTER I

INTRODUCTION

PAGE
1 Its scope—Living matter—Metabolism—Up and down—Food and energy—Supply—Expenditure—Death—Organisation.
2 The tripod of physiology: anatomy, chemistry, and physics—Its methods of study—The pyramid of protoplasm—Amœba to man—The composition of a man's food—The composition of a man's body—Six proximate principles—Three important elements—The proteid molecule—Proteid and protoplasm—Comparison of protoplasm, body-stuff, food-stuff, milk, and blood.
6 Oxygen and carbon dioxide.
7 Excitability.

Physiology deals with the chemical and physical changes which occur in and by living matter. Vegetable physiology deals with plants, animal physiology with animals, human physiology with man.

We cannot define 'life' in physical terms; we can, however, observe and state in what essential particulars living differs from non-living matter, or from matter which is dead.

The essential feature of living matter is its instability; it is the seat of chemical changes, collectively termed metabolism. These changes are divisible into—1. Constructive, integrative, anabolic, or synthetic processes, in the course of which non-living matter is annexed or assimilated by living matter; 2. Destructive, disintegrative, katabolic, or analytic processes, in the course of which living matter and storage substances are expended.

Living matter is supplied by food, the potential energy of which is utilised in the course of analytic changes. These changes mainly fall upon storage substances, and only involve living substance to a very small extent; otherwise expressed the greater portion of the food is consumed under the influence of living substance without ever forming an integral part thereof.

At any given moment a living body, considered simply as a mass of living matter, possesses a fund of potential energy derived from the previous storage and assimilation of foreign matter; this potential or stored-up energy is constantly flowing off in the form of actual energy as heat and as mechanical work; it is constantly replenished by the continued assimilation of foreign matter. Sooner or later restoration ceases, energy runs down, and the living body ceases to live.

But a living body is not merely a homogeneous mass of living matter; the living matter or protoplasm has become differentiated and organised, and it has surrounded itself with protoplasm products. The lowest form of living matter is a simple cell, *e.g.* an amœba or a leucocyte. The highest form of living matter is the human body, which is literally a 'nation' of cells derived from a single cell called the ovum, living together, but dividing the work, transformed variously into tissues and organs, and variously surrounded by protoplasm products.

Human physiology, or the knowledge of the functions of the cells, tissues, and organs which constitute the body, requires, in the first place, an elementary knowledge of anatomy, of chemistry, and of physics. By anatomy, including microscopical anatomy, we learn what the cells, tissues, and organs are like, where they are situated, what channels lead to and from them. By chemical methods we learn what they are composed of, what they make, and what their products can do. By physical methods we learn what work they do in and out of the body, and how their functions are modified by external forces.

Given these three essentials, physiological processes and consequences are studied by exact observation and by insulative experiment, upon the lower animals, upon the higher animals, and upon man. The lower animals, the frog in particular, are especially suitable to the study by direct experiment, of the function of isolated tissues, such as nerve and muscle. The higher animals—rabbit, cat, dog, horse, monkey, &c.—are required for the study of organs which are anatomically similar to those of man. On man we carry out such experiments as require intelligent co-operation on the part of the subject, and we record exact observations concerning the natural history of disordered functions, and the effects upon such functions of various remedial interferences.

We have to bear in mind that the complicated functions of the human body are at the apex of the physiological pyramid, the functions of the simple protoplasmic cell at its base. The following general facts apply throughout the entire pyramid; they are observable in the everyday life of a man; they are logically attributable to the smallest lump of protoplasm, such as a single white blood-corpuscle.

Let us first consider the facts nearest to our hand:—The composition of a man's food. The composition of a man's body.

The following articles—*meat* (with *fat*), *bread*, *salt*, *water*, and the *air* we breathe—contain representatives of all the various classes of proximate principles which must enter a man's body to keep that body living and energy-yielding. The meat contains the proximate principles[1] *proteid* and *fat*. The bread contains *carbohydrate*; to these are added *salt* and *water*, and from the air *oxygen*. These six proximate principles constitute the essential income of all living matter—of each microscopic speck of protoplasm as of the entire animal body. The three most important elements which they contain are *oxygen*, *nitrogen*, and *carbon*.

Oxygen we need not at present consider beyond remarking that it is a simple element, a gas, which easily finds its way into and is assimilated by living matter.

Carbohydrates, *Fats*, and *Proteids* are the three groups which most demand our attention at this stage. They all contain the elements, carbon, oxygen, and hydrogen; proteids contain in addition the element nitrogen. The entire nitrogen income is contained in proteids; the chief carbon income is supplied in carbohydrates and fats. A glance at their formulæ shows further some noteworthy points.

---

[1] A proximate principle is any element or group of elements which can be separated as such without decomposition from animal or vegetable bodies.

The formula of the carbohydrate, dextrose, is $C_6H_{12}O_6$. All carbohydrates, in common with dextrose, contain no nitrogen, and they contain hydrogen and oxygen in proportion by volume to form water, viz. $\frac{2\text{ hydrogen}}{1\text{ oxygen}}$. If a carbohydrate is burned, *i.e.* completely oxidised, it requires additional oxygen from outside itself only for the carbon; the amount of oxygen in the carbohydrate itself is sufficient for the complete oxidation of the hydrogen it contains.

The formula of the fat, tripalmitin, is $C_{51}H_{98}O_6$, or $C_3H_5,3(C_{16}H_{31}O_2)$. Fats contain no nitrogen; they contain, relatively to the proportion $\frac{2\text{ hydrogen}}{1\text{ oxygen}}$, a great deal of hydrogen, very little oxygen. In tripalmitin, for instance, the proportion is $\frac{13\text{ hydrogen}}{1\text{ oxygen}}$. To be completely oxidised, fat requires outside oxygen to satisfy hydrogen as well as carbon.

The formula of a proteid is given as $C_{72}H_{112}N_{18}O_{22}S$, but this is not a true chemical formula, proteids, however pure, being of variable composition. We see, however, by this approximate formula that a proteid contains nitrogen, and that the proportion between hydrogen and oxygen is greater than in starch, less than in fat, viz. $\frac{5\text{ hydrogen}}{1\text{ oxygen}}$. By weight the percentage composition of various proteids is

$$\text{C.}\begin{cases}51\cdot5\\ \text{to}\\ 54\cdot5\end{cases}\qquad \text{H.}\begin{cases}6\cdot9\\ \text{to}\\ 7\cdot3\end{cases}\qquad \text{N.}\begin{cases}15\cdot2\\ \text{to}\\ 17\end{cases}\qquad \text{O.}\begin{cases}20\cdot9\\ \text{to}\\ 23\cdot5\end{cases}$$

Moreover, the proteid molecule holds to itself, if not within itself, small, but important, quantities of *sulphur*, of *phosphorus*, and of *iron*. There is sulphur in every proteid, however pure; there is phosphorus in most; there is iron in one most important compound, hæmoglobin.

A proteid molecule is very large and composed of a large number of atoms of C. O. H. N.; these may 'hold hands,' so to speak, in many different ways; the molecule, while forming part of protoplasm, may take many shapes, may offer many kinds of opportunities for different kinds of chemical intercourse. It is to this character that the proteid molecule owes its preponderating importance in living matter; the molecule, while in living matter, is 'all alive,' the seat and centre of an active commerce of atoms. The relation between proteid and protoplasm is very close; proteid, as we examine it chemically, is non-living, protoplasm is living; if we attempt to examine protoplasm chemically we necessarily kill it in the attempt. But if, having killed protoplasm, we continue the chemical examination, we find that the killed matter is mostly proteid and water. It appears that water is an integral part of protoplasm. Pushing the examination still further, we find that our killed protoplasm contains a small proportion of carbohydrate, a small proportion of fat, and a small proportion of salts.

Thus we have found, in the analysis of protoplasm, that its main bulk is composed of water and proteid, that it also comprises some carbohydrate, some fat, and some salt. And by this different channel we are brought to our starting-point. The list just given is the same as that already given of the proximate principles required to keep a man alive, with the one exception of oxygen, which we did not find in our analysis of dead protoplasm. This exception is, however, easily accounted for; we shall find that a supply of oxygen is necessary to protoplasm, but that we need not expect to find any free oxygen left in killed protoplasm. We may sum up these considerations in the following form:—

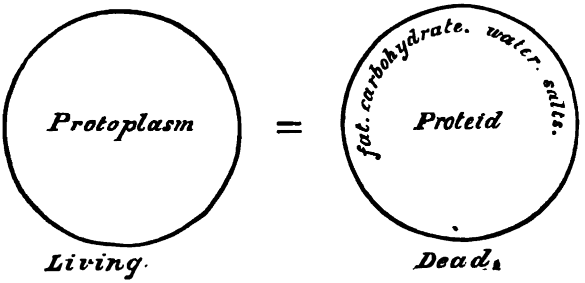


FIG. 1.

The chemical elements contained in the proximate principles above considered are C. O. H. N. They enter the body in *proteids*, *fats*, and *carbohydrates*, and together with *water*, *salts*, and free *oxygen* they concur to the formation and maintenance of *protoplasm*.

Knowing what goes into the body, we have a general knowledge of its composition; its chief component elements will be C. O. H. N; its chief component proximate principles will be carbohydrates, fats and proteids, water and salts.

Water forms at least $\frac{2}{3}$ the total body-weight. A human body weighing twelve stone, if completely dried would weigh about four stone. The proportion of water varies in the various tissues and fluids; it is greatest in the saliva and in gastric juice, least in the enamel of the teeth, but even in bones the proportion is considerable. The following are representative numbers:—

	Water per 1,000	Solids per 1,000
Saliva	995	5
Gastric juice	973	27
Milk	891	109
Blood	791	209
Muscle	757	243
Bone	486	514
Enamel of teeth	2	998

Salts are contained in all the tissues and fluids. The principal salts are:—sodium chloride, in the fluids especially; potassium phosphate, in the tissues especially; calcium phosphate, in bone particularly. The above (viz. water and salts) are the chief inorganic compounds; the organic compounds are *proteids*, *fats*, and *carbohydrates*, which we have considered sufficiently at the present juncture, but shall refer to again hereafter. We may now realise the essential similarity in the composition of protoplasm with that of the entire human body, and of its normal food-supply. Each comprises the same elements and the same proximate principles; we shall find that *milk*, which is the sole food in early life, and *blood*, which is the general food of the whole body—and during gestation the fund from which a new body is entirely formed in the mother's womb—likewise comprise the proximate principles enumerated above.

Oxygen.—We have left for separate consideration this necessary item of supply. A man must breathe to keep alive; protoplasm runs down and dies if deprived of oxygen. The tissues of the human body get oxygen from the blood, which gets it by the lungs. The blood is oxygenated at the lungs, deoxygenated or reduced by the tissues. Protoplasm gets oxygen from the air, or from oxygen-holding compounds which it can decompose. This deoxygenating or reducing action of protoplasm is a fundamental characteristic of the living state. Living matter requires oxygen, and gets it from the air, or by taking it away from combinations which do not hold it fast. Although oxygen is continuously necessary to living matter, we do not at any given moment find free oxygen in protoplasm or in tissue. It is at once drawn into chemical combination. It reappears afterwards in company with carbon, as *carbon dioxide*, which must be discharged. A man exhales carbon dioxide, protoplasm exhales carbon dioxide. But, as we shall see hereafter, the carbon dioxide comes, not from any direct union of free oxygen with free carbon, but indirectly from complex compounds in which the incoming oxygen had become stored.

The signs by which we can always recognise that protoplasm is alive are—(1) its reducing or deoxygenating power, (2) its exhalation of carbon dioxide, (3) its **excitability**. The first two tokens have just been considered. The third—**excitability**—manifests itself as movement in response to excitation, and will claim our attention more particularly when we come to the study of the nervous system. At this stage it will be sufficient for us to recognise 'excitability' as a fundamental property of living matter.

CHAPTER II

THE BLOOD

PAGE

9 **Function and composition:** Proximate principles—Elements.

9 **Physical properties:** Consistence—Colour—Opacity—Specific gravity—Reaction—Taste—Smell—Coagulability.

11 **Microscopic structure:** Corpuscles—Red and white—of mammalia, non-nucleated, biconcave, and circular—of amphibia &c., nucleated, biconvex, and oval—Leucocytes—Numeration of blood-corpuscles.

12 **Plasma—Serum—Fibrinogen—Fibrin:** Preparation of serum—of fibrin—of defibrinated blood—of plasma—* Centrifugal apparatus—Magnesium sulphate plasma—Cold plasma—Peptone plasma—Buffy coat—Lake blood.

14 **Quantity of blood in the body.**

15 **Chemical composition:** The blood gases—* The mercurial gas-pump—Differences between arterial and venous blood—Gas—Colour—Hæmoglobin—Arterial blood is of uniform, venous blood is of variable composition—Hepatic blood has more sugar—Portal blood may contain products of digestion—Blood from glands (kidney, submaxillary)—Blood from muscles—Temperature—Cooled venous blood—Warmed venous blood—Splenic blood.

20 **Composition of the blood in disease:** Anæmia—Leucocythemia—Inflammatory blood—Diseases of the kidney—Gout—Diseases of the liver—Diabetes—Hæmophilia.

21 **The life-history of the blood-corpuscles:** The red corpuscles—Origin—Function—End—The white corpuscles—Origin—Vital characters—Functions—Emigration—Suppuration—Cicatrisation.

25 **Hæmoglobin—Its compounds and derivatives:** Characters—Crystalline and indiffusible—Oxyhæmoglobin—Reduced hæmoglobin—Carboxyhæmoglobin—Nitroxyhæmoglobin—Various modes of reduction—* The derivatives of hæmoglobin; normal, abnormal, and artificial—*Normal*: bile and urine pigments—*Abnormal*: hæmatoidin—Methæmoglobin—Hæmatin—'Smoky' urine of hæmaturia—'Coffee-ground' vomit of hæmatemesis—*Artificial*: Methæmoglobin—Acid hæmatin—Alkaline hæmatin—Reduced hæmatin or hæmochromogen—Hæmatoporphyrin—Hæmin—Estimation of hæmoglobin.

31 * Identification of spectra—Preparation of suitable solutions.

32 **Tests for blood:** By the microscope—by hæmin crystals—by the spectroscope—by guaiacum and hydrogen peroxide.

34 **The composition of plasma, serum, lymph, and serous fluids—Coagulation—
Facts and theories:** Plasma—Serum—Lymph—Chyle—Serous effusions—
Their varieties—Classical experiment—Buchanan—A. Schmidt—Hammar-
37 sten—* Methods of separating the proteids of plasma and of serum—Pre-
paration of fibrinogen from plasma by NaCl—of paraglobulin from serum by
39 $MgSO_4$—of fibrin-ferment—of serum-albumin—Influence of the vessels
upon coagulability—Normally the blood remains fluid while in the vessels
—Blood contained in excised vessels—Extravasated blood—Abnormally
blood may coagulate in the vessels—Thrombosis—Experimental thrombosis
—Abnormally the blood may fail to coagulate after removal from the vessels
—Peptone—Leech extract.

A REGULAR supply of healthy blood is an essential condition of the life of the animal body, and of its several parts. The whole body dies if blood be lost in excessive quantity; a single organ, or a single limb, dies if its supply of blood be permanently arrested. The blood is the medium of nourishment to the tissues of the body, and contains, therefore, the materials which they require, viz. *oxygen*, *water*, *proteids*, *carbohydrates*, *fat*, *salts*. Living tissues are constantly in a state of chemical change, consuming and assimilating to themselves materials which they derive from the blood, and rejecting the consequent waste products. These are discharged into and carried away by the blood, which contains, therefore, the materials in their used-up form, viz. *carbonic acid* and *urea*.

In correspondence with the large proportion of proteids and of hæmoglobin contained in blood, the elementary composition of its solid residue agrees closely with that of proteids in general, and with that of muscle, which is essentially proteid. A comparison of some actual analyses, giving the amounts of the chief elements entering into the composition of blood, muscle, hæmoglobin, and proteids, will best illustrate this similarity.

Elementary composition (in the dried state)	of Blood	of Muscle	of Hæmoglobin	of Proteids
Carbon . . .	51·96	51·86	53·8	51·5 to 54·5
Oxygen . . .	21·30	21·30	21·2	20·9 to 23·5
Hydrogen . .	7·25	7·58	7·1	6·9 to 7·3
Nitrogen . . .	15·07	15·03	16·1	15·2 to 17

Physical properties.—Blood in the body, or freshly drawn, is, a slightly *viscid* fluid, bright *scarlet* in colour if taken from an artery, dark purple or *almost black* if taken from a vein; in either case *opaque*, even in thin layers. It is heavier than water, its *specific gravity* being about 1,050 as compared with water, 1,000 —*i.e.* 1,000 cubic centimeters of water weigh 1,000 grammes, 1,000 cubic centimeters of blood will weigh about 1,050 grammes;[1]

---

[1] Measurements will be given throughout according to the metric system.

1 gramme = about 15 grains.

100 cubic centimeters, or 100 c.c. = about 3½ fluid ounces.

For microscopic measurements the unit is the micromillimeter, or $1\mu = \frac{1}{1000}$ millimeter = about $\frac{1}{25000}$ inch.

The preliminary difficulties generally experienced by students in the use of metric measurements are soon overcome, and their greater simplicity appreciated. The relative magnitudes 8μ, 10μ, 15μ, 50μ are far more readily realised than the corresponding values $\frac{1}{3200}$ in., $\frac{1}{2540}$ in., $\frac{1}{1690}$ in., $\frac{1}{500}$ in., and no student who has its reaction is *alkaline*, never acid—the popular expression ‘acidity of the blood’ has no foundation in fact. The alkalinity varies in degree; it is at a maximum after meals, owing to the secretion of acid gastric juice, and at a minimum after severe exertion, owing to the acid which is formed in muscular contraction; the alkalinity of blood is attributable to the presence of disodic phosphate—Na_2HPO_4, and the degree of alkalinity is normally the same as that of a ·3 per 100 solution of sodium carbonate. The *taste* of blood, in consequence of the presence of sodium chloride, is saltish, and it possesses a faint and indescribable smell, which is made more distinct by the addition of a few drops of sulphuric acid. The property which is the distinguishing characteristic of blood is its *coagulability*. Left undisturbed for a few minutes after it has been drawn, the fluid blood becomes more and more viscid; in a few minutes it is no longer a fluid, but a red jelly; as time goes on, the jelly shrinks and gets firmer and squeezes out drops of almost colourless liquid; in a few hour the jelly has shrunk to its utmost, and floats in a considerabl quantity of the liquid. Coagulation has taken place and is no complete, the shrunken jelly is the *clot*, the liquid in which i floats is the *serum*; coagulated blood consists of clot and serum.

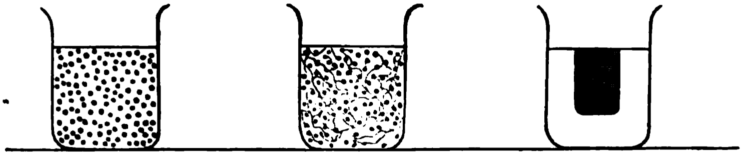


FIG. 2.—DIAGRAM TO ILLUSTRATE THE PROCESS OF COAGULATION.

I. Fresh. (Corpuscles and plasma.)
II. Coagulating. (Birth of fibrin.)
III. Coagulated. (Clot and serum.)

Plasma minus fibrinogen equals serum. Corpuscles plus fibrin equals clot.

The process of coagulation is hastened by moderate warmt and by contact with foreign bodies; it is retarded by cold, b certain salts (sodium and magnesium sulphate in particular), an when the blood is protected from contact with foreign bodies b means of oil (with which it does not come into actual contact Blood which has been frozen before coagulation has taken plac

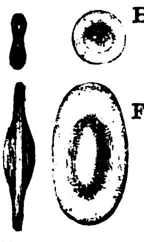
---

once made up a five per cent. solution by weighing out five grammes of a solid in 100 c.c. of water will ever wish to employ grains to the ounce.

The capacities of vessels used in the practical classes are marked on the metr system, and students soon learn that a 100 c.c. flask holds rather less than 4-oz. bottle, and that a 500 c.c. beaker is the equivalent of a very short pint.

may be so kept for months, and yet will clot when thawed; this fact implies that coagulation is not a vital act, but only a physicochemical change.

Microscopic structure.—A small drop of blood obtained by pricking the finger, and quickly covered for examination under the microscope, is seen (with a magnifying power of 300 diameters) to be composed of a multitude of corpuscles floating and rolling over and over in the minute eddies of a fluid which is not itself visible—the liquor sanguinis or plasma. Examined more closely the corpuscles will be seen to be of two kinds—the coloured corpuscles the more numerous, and the white corpuscles, far fewer in number, 2 or 3 of the latter among 1,000 of the former, so that they require to be looked for with some little care. All the more so that the tint of the coloured corpuscles is faint, they are not far from colourless, and it is only by their great number that the strong red colour of blood is produced. On still more careful examination with very high powers, very small colourless corpuscles—μ in diameter, 2 or 3 to every 100 red corpuscles—may be distinguished; these are called blood-platelets or hæmatoblasts. A single coloured corpuscle seen flat is circular, and, as the microscope is focussed up and down with the fine adjustment, appears now as a dark centre surrounded by a light ring, now as a light centre surrounded by a dark ring. This appearance is not due to a nucleus; human blood-corpuscles, in common with those of all mammalia, have no nucleus. The appearance is due to the cupped shape of the corpuscles, a single corpuscle seen sideways looks something like a dumb-bell, and the two views combined show that the actual shape of the corpuscle is that of a disc cupped on both surfaces—a bi-concave disc; these discs frequently run together and adhere to each other in longer or shorter rolls like piles of coins. The blood of amphibia, reptiles, fishes, and



Human blood-corpuscles, side and front view.

Frog's blood-corpuscles, side and front view.

FIG. 3.

The corpuscles are drawn to the same scale, viz. × 1000. 1μ or $\frac{1}{1000}$ mm. of actual length is represented by 1 mm.; the human corpuscle as sketched above is 7 mm. in diameter, *i.e.* its actual diameter is 7μ; the frog's corpuscle is 20μ by 11μ. The corpuscles of mammalia resemble those of man, but differ in size. Average magnitudes are: elephant, 9μ; dog, rat, 7μ; cat, horse, ox, 6μ; goat, sheep, 5μ. But the corpuscles of man, averaging 7μ, may range from as low as 5μ to as high as 9μ.

birds has corpuscles different from those of mammalian blood in shape and structure. Of all these lower classes the red corpuscles are oval, convex on both sides, and their central part differs in structure from the remainder of the corpuscle, constituting a nucleus.

Various instruments have been devised for enabling an estimate to be formed of the number of corpuscles present in a given volume of blood; the principle of all such instruments is to furnish the observer with a very minute cubic space under the microscope, in which it is possible to see and count the corpuscles of blood diluted a given number of times. The form of instrument most used in this country has been called a hæmacytometer (Gowers); the blood is diluted 200 times, and observed through the microscope in a cell $\frac{1}{5}$ millimeter deep, and divided into $\frac{1}{10}$ millimeter squares: the cubic space of each division is thus $\frac{1}{500}$ millimeter, and the number of corpuscles in one division multiplied by 100,000, gives, therefore, the number of corpuscles per cubic millimeter. Normally, this number is 4,000,000 to 5,000,000 (40 to 50 in each square); abnormally, in extreme anæmia, it may be as low as 1,000,000 to 2,000,000 (10 to 20 in each square).

The white corpuscles—also called leucocytes—are of all shapes while they are alive, and their shapes are constantly, but very slowly, changing; ultimately—*i.e.* as they die—they assume a globular form. Many of them break up and vanish. They are variable in size, some are no larger than the coloured corpuscles, some are even smaller, but typical leucocytes are about twice the size of a coloured corpuscle. They look granular, some being coarsely granular, some finely granular, and they often contain foreign particles.

Plasma, serum, fibrinogen, fibrin.—The fluid in which the corpuscles float while the blood is uncoagulated is called the *plasma*, or *liquor sanguinis*. It differs from the fluid in whic the clot floats after the blood has coagulated, *i.e.* the serum, i this important respect, that plasma contains a body called *fibri-nogen*, while serum contains no fibrinogen. Fibrinogen is, a its name implies, a body which becomes or gives rise to fibrin It is the conversion of fibrinogen into fibrin which is th essential event in the coagulation of the blood. Fibrinogen i the plasma becomes fibrin, which pervades the fluid in all direc-ions in the form of innumerable filaments; the plasma havin lost fibrinogen, serum is left. The filaments of fibrin shrink, and, entangling in their meshes the corpuscles, sweep these from the serum, and form with them the clot, which gradually shrinks and squeezes out the serum. To obtain *serum* it is only necessary to allow freshly drawn blood to coagulate without disturbance.

To obtain *fibrin*, blood is whipped with a bundle of twigs as soon as it is drawn; the fibrin adheres to the twigs, and forms a stringy mass, which is to be subsequently washed in water and left under a running tap until almost white. The whipped blood from which fibrin has been separated is '*defibrinated' blood.*

To obtain *plasma*, it is necessary to prevent coagulation, so that the corpuscles may subside and leave an upper layer of plasma. To this end, the blood is allowed to flow into a vessel surrounded with ice, and containing a saturated solution of magnesium sulphate. After a few hours the corpuscles will subside if the vessel is left undisturbed, or if, instead of leaving the separation to take place by the action of gravity, the vessel is fixed to a horizontal wheel revolving at a high speed, the separation will be much accelerated by centrifugal force.

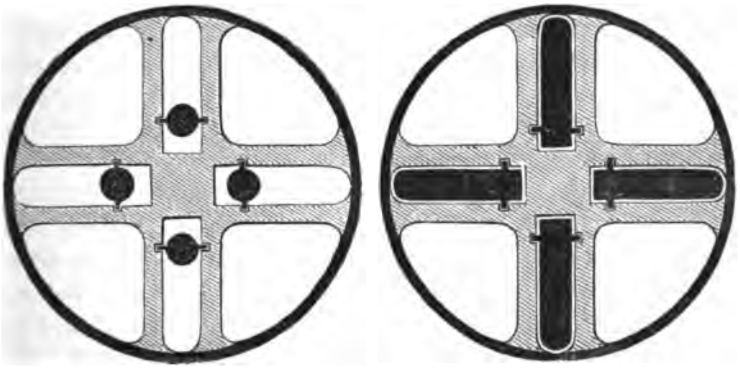


FIG. 4.—PLAN OF CENTRIFUGE AS USED FOR THE SEPARATION OF PLASMA.

Centrifugal Apparatus. Disc fitted with four long buckets pivoted so that they hang vertically when the disc is at rest, and assume a horizontal position as the disc revolves. Large test-tubes containing the blood-mixture fit into the buckets. By centrifugal force, while the disc is revolving, the corpuscles collect towards the circumference, *i.e.* at the bottom of the test-tubes; the plasma is left nearer the centre, *i.e.* at the top of the test-tubes.

Stationary. The buckets (represented in transverse section) hang vertically from the disc.

Revolving. The buckets (represented in longitudinal section) swing out to a horizontal plane.

It is not always necessary to employ both ice *and* magnesium sulphate. From blood mixed at once with magnesium sulphate at ordinary temperature, plasma can be obtained by subsidence, or by the centrifuge. By cooling blood sufficiently rapidly, and leaving it to stand surrounded by melting ice, plasma may be obtained without magnesium sulphate. Horse's blood, which coagulates more slowly than that of other mammals, is the best kind of blood to choose for the purpose.

Plasma is coagulable; magnesium sulphate plasma coagulates after addition of an equal bulk of water; cold plasma coagulates as soon as it ceases to be cold, *i.e.* at ordinary room temperatures (12° to 20° Cent.).

Another convenient method of obtaining plasma is afforded by the property which commercial peptones possess of preventing coagulation when they are injected into the vessels (pp. 40 and 186). The blood of an animal so treated does not coagulate after it is drawn, and plasma may be obtained from it by the centrifuge.

The upper part of the clot which forms in normal horse's blood is not red like the lower portions, but pale or buff-coloured. This difference is due to the fact that the red corpuscles of horse's blood cling together in little clumps which quickly subside from the upper part of the fluid, and the clot which forms subsequently is comparatively free from them. A buffy coat has also been noticed in human blood in inflammatory conditions; the coagulation of normal human blood is too rapid to allow of the formation of a buffy coat, but inflammatory blood coagulates more slowly, and the upper part of the clot is left pale.

Defibrinated blood is opaque, and viewed by reflected light it is red. After an equal volume of distilled water has been added, it becomes translucent, and viewed by reflected light it is of a dark lake colour. The difference is owing to the action of water on the red corpuscles; the hæmoglobin has been dissolved, and, leaving the stroma, has become diffused throughout the fluid; the colourless stromata permit the transmission of light through the fluid, and less light is reflected from it. Hence it is translucent when viewed by transmitted light, dark lake-coloured when viewed by reflected light. Blood may be 'laked' by other means than water—*e.g.* by alternate freezing and thawing, by chloroform, by bile-acids.

Quantity of blood in the body.—The total amount of blood has been estimated to be in man about $\frac{1}{13}$ of the body-weight, *i.e.* five to six litres (or rather more than one gallon). From this datum, and from those given in the next paragraph, we may form a rough notion of the absolute amounts of the various proximate principles in circulation in the blood, viz. about 500 grammes hæmoglobin, 450 grammes proteids, 2·5 grammes iron, &c.

The total amount is distributed in the body approximately as follows:—$\frac{1}{4}$ in the thoracic viscera; $\frac{1}{4}$ in the muscles; $\frac{1}{4}$ in the liver; $\frac{1}{4}$ in remaining parts. It is estimated by collecting all the blood that escapes when an animal is bled to death, subsequently washing out the vessels with salt solution, finally mincing and washing the organs. The amount of blood in these two washings is found, by comparison of their red tint with the tint of a sample of blood of known dilution; the comparison is facilitated by the previous passage of carbonic oxide through the fluids. For example, a dog weighing ten kilogrammes is bled, and yields 400 c.c. of blood; the vessels are washed out and the various tissues are minced and washed; the united bulk of the washings is five litres, and the tint is found to be equal to that of one c.c. of blood fifty times diluted, *i.e.* the five litres contain $\frac{1}{50}$ of blood=100 c.c. The total amount of blood is therefore 500 c.c., that is to say, $\frac{1}{20}$ the weight of the dog.

The estimation of the blood in particular organs is determined in a similar manner, the vessels having been previously ligatured before the cessation of circulation.

Chemical composition.—100 grammes of blood consist of about 80 grammes of water, 20 grammes of solids, some in solution, some in suspension, and contain 50 cubic centimeters of gases, some in solution, some in loose chemical combination with other constituents of the blood.

The twenty grammes of solids comprise:—

Hæmoglobin	10 grammes
Proteids	9 "
Fat Carbohydrate Salts Urea	1 "

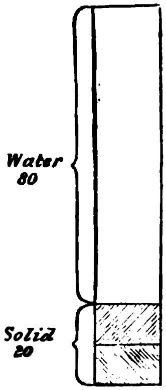


FIG. 5.—THE PROPORTION OF SOLIDS TO WATER IN THE BLOOD GRAPHICALLY EXPRESSED.

The important proteid, *fibrinogen*, forms only a very small proportion of the total proteid, although the fibrin which it forms appears of considerable bulk when it is separated by whipping, yet its actual weight is small—1,000 grammes of blood yield about 2 grammes of fibrin. The *hæmoglobin* is contained in the coloured corpuscles. The proteids comprise *serum-albumin* and *serum-globulin* in about equal proportions dissolved in the plasma.

Physically considered, 100 grammes of horse's blood consist of about:—

Corpuscles	33 grammes
Plasma	66 „

The 33 grammes of corpuscles comprise:—

Water	22 grammes
Solids (chiefly hæmoglobin)	11 „

This, indeed, gives a low estimate for hæmoglobin, its average amount in human blood being between 10 and 15 per 100.

The 66 grammes of plasma comprise:—

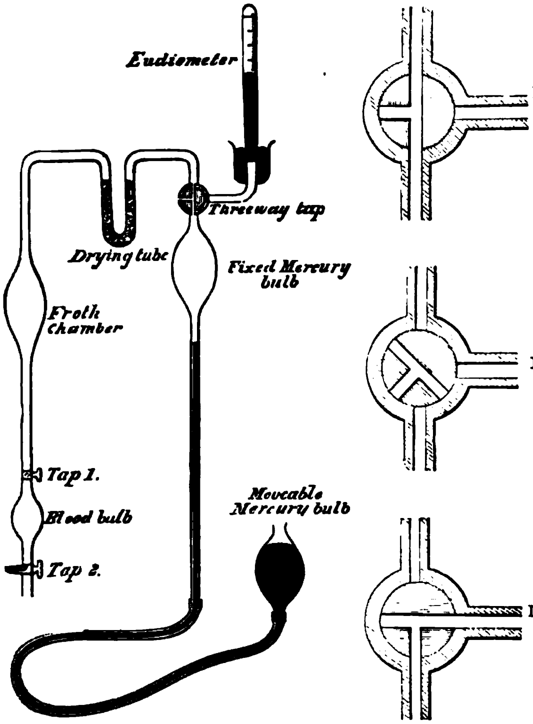
Water	60 grammes
Solids { Serum-albumin Serum-globulin }	6 „

The chief *salts* of the blood are chlorides and phosphates, combined with sodium and potassium. Sodium chloride preponderates in the plasma; potassium phosphate preponderates in the corpuscles. Other salts present are sulphates and sodium bicarbonate ($NaHCO_3$).

Fat, sugar, and *urea* are constantly present in the blood, but in small quantities only. Fat is present in variable quantity; after a meal of fat it may be so abundant as to form a scum on the surface of drawn blood; it remains, however, but a very short time in circulating blood, being separated by the tissues and stored in them; 1,000 grammes of blood contain from 2 to 6 grammes of fat. Sugar is present in small but constant quantity; 1,000 grammes of blood contain about 1 gramme of sugar Urea is present in small quantity; 1,000 grammes of blood contain about ¼ to ½ gramme.

100 c.c. of blood contain between 50 and 60 c.c. of th gases *oxygen* and *carbon dioxide.* These gases are present i small proportion simply dissolved, but for the most part in state of loose chemical combination, from which they can b separated by subjecting the blood to a vacuum. Oxygen i held by the red corpuscles in combination with hæmoglobin as oxy-hæmoglobin; carbon dioxide is held by the plasma i combination with soda, as sodium carbonate (Na_2CO_3) and sodiu bicarbonate ($NaHCO_3$). In both cases the combination is ve feeble; it is easily unmade, and as easily re-made. By simpl

subjecting blood to a vacuum, gases, relieved from atmospheric pressure, are disengaged and may be collected; by adding a reducing agent to the blood, oxygen is withdrawn from combination with hæmoglobin, which remains therefore as reduced hæmoglobin. A reducing agent in relation to blood is any com-



I. The froth chamber is in communication with the fixed mercury bulb.

II. All communications are closed.

III. The fixed mercury bulb is in communication with the eudiometer.

Fig. 6.—Plan of Mercury Pump for the Extraction of the Gases of the Blood.

Two glass bulbs containing mercury; one is fixed, the other can be raised and lowered. A three-way tap, which can be turned into three positions, I. II. III. A 'blood bulb,' which is filled from an artery or vein, through a tube slipped over the end of tap 2, and which can be connected with, or disconnected from, the froth chamber by opening or shutting tap 1. 'Froth chamber' serving to intercept spurts of blood when the gases are bubbling out. Vacuum is established by repeatedly lowering the movable mercury bulb while the three-way tap is in position I. and raising it with the tap in position III. The first step draws air from the apparatus into the fixed mercury bulb, the second step drives out this air by the delivery tube.

Vacuum having been established, the eudiometer filled with mercury is adjusted over the delivery tube, and the tap between froth chamber and blood bulb is opened. The blood begins to bubble and its gases are given off into the vacuum; by raising the mercury bulb (with tap as in III.) the blood-gas is discharged through the delivery tube into the eudiometer, by lowering the bulb (with tap as in I.) the extraction is repeated; by further repetition of the up and down manœuvre, and by immersing the blood bulb in water warmed to 40°, all the gas is extracted and collected in the eudiometer for further examination.

pound or element having an affinity for oxygen greater tha that of hæmoglobin: ammonium sulphide, and Stokes's fluid, are the reducing agents commonly employed; germinating yeast putrefactive bacteria and living tissues are also reducing agent inasmuch as they require oxygen, and will withdraw it from oxy hæmoglobin. A little yeast mixed with arterial blood will soo deoxidise it; decomposing blood—*i.e.* blood in which putrefacti bacteria are living and multiplying—is quickly deoxidised; an the living tissues change the blood which passes through them fro the arterial or oxygenated, to the venous or deoxygenated stat

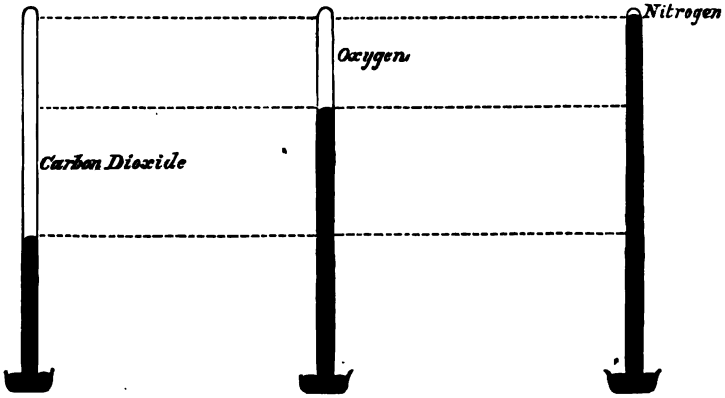


FIG. 7.—EUDIOMETER TUBES.

The gases thus obtained consist of carbon dioxide, oxygen, and nitrogen. T amount of carbon dioxide is ascertained by introducing some caustic potash into t eudiometer; the difference in the volumes of gas in the tube before and after t absorption of carbon dioxide makes known the amount of this gas. The amount oxygen is similarly ascertained by observing the diminution of volume conseque upon the introduction of phosphorus or of pyrogallic acid. The residual gas in t tube is nitrogen. The readings must be corrected for temperature and pressure.

The chief *difference between arterial blood and venous blo* —*e.g.* that in the right auricle—is that the former contains mo oxygen and less carbonic acid than the latter; this differen is accompanied with an evident difference of colour, arter blood being bright red, while venous blood is almost black, and is hardly necessary to state that the amount of oxyhæmoglob is greater in arterial than in venous blood, while the amount reduced hæmoglobin is greater in venous blood. But it wo be a mistake to suppose that *all* the hæmoglobin in arterial bl

---

[1] Stokes' fluid. To a fresh solution of ferrous sulphate, 2 grammes per 100 add 3 grammes tartaric acid; to this solution add ammonia until it is fai alkaline.

is oxyhæmoglobin, all the hæmoglobin in venous blood, reduced hæmoglobin. The difference is only in the relative amounts, as may be illustrated by the following example (Hüffner) :—

100 c.c. of dog's blood from crural artery contained:

Oxyhæmoglobin	15 grammes
Reduced hæmoglobin	2 „

100 c.c. of dog's blood from crural vein contained:

Oxyhæmoglobin	10 grammes
Reduced hæmoglobin	7 „

These figures show that arterial blood is not completely saturated with oxygen, and venous blood is not completely deoxygenated. A corresponding fact would be shown by measurements of the gases contained in arterial and in venous blood, as in the following example :—

100 c.c. arterial blood contained:

Oxygen	20 c.c.
Carbonic acid	40 „

100 c.c. venous blood contained:

Oxygen	10 c.c.
Carbonic acid	48 „

Thus arterial blood still contains carbonic acid, and venous blood still contains oxygen.

In addition to the difference in the gases, which is the most considerable, there are minor differences, among which may be named as the most important, although they are minute, the differences in the amounts of urea and sugar. Arterial blood contains more urea and less sugar than does the general venous blood.

Whereas arterial blood is of uniform composition, the same blood being distributed to all parts of the body, venous blood, returning from different parts and organs, is not uniform, but varies in accordance with the material which may have been added to or subtracted from the blood. The blood of the *hepatic vein*, coming from the liver, where sugar is constantly produced, contains a little more sugar than other blood. The blood of the *portal vein*, coming from the digestive viscera, contains products of digestion—if digestion is taking place—an excess of sugar or of fat or of proteid, if these substances are being absorbed from the intestinal tract. The venous blood of *secreting glands* is also apt to vary from the usual quality; from a gland which is in constant action, like the kidney, the blood returns in a les deoxygenated state than from a muscle, or from the brain. Th blood of the *renal veins* is not like ordinary venous blood, bu bright red, like arterial blood; and, in correspondence with the fac that the kidney separates urea from the blood, its venous bloo contains less urea than other venous or than arterial blood Other glands which are sometimes in action, sometimes at rest show corresponding differences: the venous blood of the *submaxillary gland*, which is of the usual venous quality while th gland is at rest, becomes bright red, like arterial blood, whil the gland is actively secreting. With *muscles* the reverse is th case: under ordinary conditions their venous blood is of the ordinary typical venous quality, but if it is analysed for gases durin muscular activity, it is found to be more venous than before, an both the deficit of oxygen and the excess of carbonic acid ar greater than in the blood coming from quiet muscles. Fro paralysed muscles, the blood is, on the contrary, less venous, an both the deficit of oxygen and the excess of carbonic acid are le than before. Differences of *temperature* also obtain in differe kinds of venous blood; venous blood returning in a superfici vein from an external part is cooler than the arterial blood goi to the part; thus, for instance, blood in the jugular vein is lower temperature than in the carotid artery, and the blood the crural vein is about 1° lower than that in the crural arter On the other hand, deep veins leading from active orga contain blood at a higher temperature even than that of arteri blood; of this inequality the hepatic venous blood is the b known instance—its temperature is about 1° higher than th of the blood in the aorta. The blood of the *splenic vein* contai a larger proportion of leucocytes than normal blood; in con quence of the production of leucocytes taking place in the gla

Composition of the blood in disease.—*Anæmia*, or poverty the blood, is the commonest and most widespread departu from the healthy standard, and is the invariable conseque of copious bleeding or of any kind of prolonged or debilitat disease. The popular term 'poverty of the blood' is accurat descriptive; the blood of an anæmic person is not deficient amount, but it is a weak blood, with an excess of water, an deficiency of solids, and a low specific gravity; the proportio

---

[1] The Centigrade scale will always be referred to in the text. The rela between the Fahrenheit and Centigrade scales is given in the Appendix.

red corpuscles is deficient, and the proportion of hæmoglobin in these even is deficient; contrasting the blood of a healthy person with that of a patient in extreme anæmia, there have been found for instance:—

Proportion of water	88	instead of	80 per cent.
„ „ solids	12	„ „	20 „
Specific gravity	1035	„ „	1055 „
Number of red corpuscles per cubic mm.	1 to 2	„ „	4 to 5 millions
Proportion of hæmoglobin	1 to 2	„ „	10 per cent.

from which it is evident that the deficiency is essentially a deficiency of hæmoglobin.

Leucocythæmia is a state characterised by an excessive number of leucocytes in the blood, and is usually associated with excessive growth of the spleen, or of the lymphatic glands.

According to observations made in the old blood-letting days, the blood of a person suffering from severe *inflammation* (of the lung, for instance) usually yields an excessive amount of fibrin, but coagulates more slowly, with formation of the so-called buffy or inflammatory coat.

Diseases of the *kidneys* are accompanied with anæmia, and the blood contains an excess of urea. In *gout*, the function of the kidneys is generally deficient, and the blood is consequently altered as just stated, with this additional and characteristic feature, viz. excess of uric acid.

Diseases of the *liver* very commonly cause anæmia; when the flow of bile is obstructed, bile-pigment accumulates in the blood and lymph.

The blood of patients suffering from severe *diabetes* contains an excess of sugar.

Hæmophilia is the name applied to a condition in which there is a peculiar tendency to bleeding, which it is difficult to check. The blood of persons subject to this affection ('bleeders') is said to be deficient in fibrin.

The life-history of the blood-corpuscles.—The *red corpuscles* make their first appearance in the embryo as the daughter cells of branched connective-tissue cells which become modified into vessels. These *embryonic corpuscles* are nucleated, they multiply by cell-division, and give rise to non-nucleated corpuscles of the adult form. In the human embryo, up to the end of the first month, all the red corpuscles are nucleated; by the end of the third month, only 10 to 20 per cent. of this number are nucleated; at birth all are non-nucleated, as in the adult. The supply of red corpuscles is kept up in the adult, (1) from the *red marrow of bone*, from which arise nucleated red corpuscles (Neumann's cells) resembling those of the embryo, (2) from the leucocytes or lymph-corpuscles, which are themselves derived from lymphatic glands and tissue, and from the spleen, (3) from the so-called blood-platelets (Bizzozero), or hæmatoblasts (Hayem), and from elementary particles (Zimmermann), the derivation of all of which is obscure. Of these various sources that first named, viz. the marrow of bone, is the most important and best attested; the derivation of red corpuscles from leucocytes, &c. is a supposition rather than an

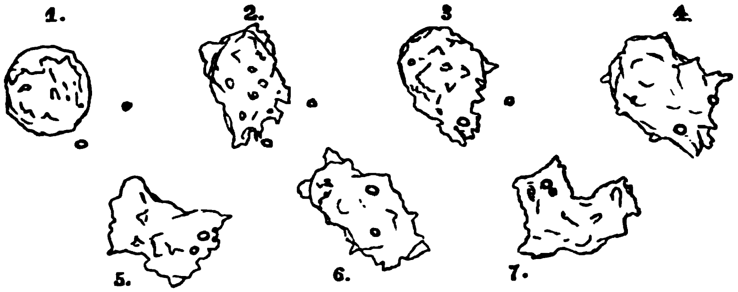


FIG. 8.—AMŒBOID MOVEMENTS.

Changes of form of a white corpuscle of newt's blood. Ingestion of two sma starch granules, and their changes of position within the corpuscle.—Quain's 'An tomy.'

observed fact. The function of red corpuscles depends upon tl hæmoglobin they contain, by virtue of which they are oxyge carriers to the tissues; their length of life has been estimated t be from two to three weeks, the estimate, which is necessari very rough, being based upon a comparison of the amount pigment which appears in bile, urine, and fæces, with the tot amount of hæmoglobin from which these pigments are derive The chief known or surmised seats of the destruction of red co puscles in the adult are the spleen and liver.

The *white corpuscles* arise from lymphoid tissues generall (lymphatic glands, adenoid tissue, spleen), where they multip by cell-division. They exhibit several fundamental life-chara ters, and several definite observations have been made whi show that they play an important part in growth, in absorptic in disintegration, and in repair. They are excitable and contra tile, they can move spontaneously by slow protrusions and retractions, in a manner quite similar to that in which amœbæ are observed to alter shape and change position, hence their movements are termed *amœboid*. They can surround particles of matter with which they come in contact, and carry them as they move from place to place. They may attach themselves to the walls of the minute veins, penetrating them, and escaping into the surrounding tissues (*emigration* or *diapedesis*), where they may accumulate and form an abscess, or become organised and form new tissue. They are possibly agents in the absorption of fat, acting as carriers from the epithelial surface of the intestine to the lacteals of the villi; in the lungs they are certainly carriers of foreign particles that may have been inhaled; it is by their agency that particles of inhaled coal-dust may be conveyed to, and deposited in, the pulmonary lymphatic glands; in the intestines, and possibly in other parts, they 'englobe' and destroy deleterious microbes. The part they play in the production of fibrin-ferment is another important point in the life-history of leucocytes, as we shall find when we come to consider coagulation.

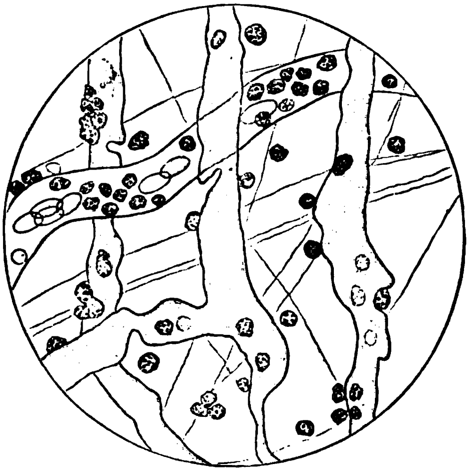


FIG. 9.—EMIGRATION OF LEUCOCYTES.

Vessels of the inferior surface of the frog's tongue as they appear after the escape of the corpuscles, filled with stationary blood, deformed and indented at the points of escape, near which the corpuscles are generally found. A portion of a vessel with an internal current is likewise seen with discs and internal and external corpuscles.—After Waller. *Phil. Mag.* 1846. 'Microscopic Observations on the Perforation of the Capillaries by the Corpuscles of the Blood.'

Of the various facts above enumerated, that which is of widest significance is the *emigration of leucocytes.* When there is irritation of a part there is a determination of blood to that part ('ubi stimulus ibi affluxus'), the vessels dilate and become congested, and the leucocytes in particular adhere to the vessel-walls, accumulate there, and begin to emigrate. With excessive irritation or peculiar debility of the part, the change exceeds congestion, and is termed inflammation; with inflammation of sufficient severity, or with tissues of unusual debility, the emigrant cells may overmaster and destroy tissue, gathering into large accumulations of cells which are now called pus-cells, and forming abscesses, the contents of which must be evacuated. A pimple which comes to a head illustrates this process on a small scale, the 'matter' which escapes when the pimple bursts or is pricked is composed of pus-cells which are emigrated leucocytes, indistinguishable from them under the microscope, and exhibiting, like them, amœboid movements.

Emigrated leucocytes may, however, play another part and effect repair of tissues: a clean, healthy wound becomes in a few hours covered with a layer of lymph, which is mainly composed of emigrated leucocytes. This exudation of lymph is the first step towards healing; if repair progresses in a healthy manner, the leucocytes may become organised and converted into connective tissue, forming the cicatrix by which the wound is closed.

Finally, we recognise as possible and probable (though the fact is not proved by direct observation), that emigrant leucocytes play a part abnormally in the production of many tumours, as well as normally in the natural growth of tissue.

To sum up—let us imagine that several leucocytes start in life together from lymphoid tissue and get into the blood. One leucocyte may get attached to a vessel of an inflamed part, may pass through it and go to the bad as a pus-cell, the constituent of an abscess: another may escape at the surface of a wound and settle down as a connective-tissue cell, the constituent of a cicatrix: a third may play the part of scavenger, and remove a foreign particle or destroy a microbe.

These are suppositions, but suppositions which have reasonable foundation in observed facts, of which amœboid movemen and emigration are the parent facts: leucocytes have been made to take up coloured granules, and by this means subsequently identified as pus-cells in an inflamed cornea; their be haviour towards microbes has been watched under the microscope; they have been found crowding round foreign bodies which are becoming absorbed or surrounded by a false membrane. But the actual transformation of leucocytes into connective tissue is not an observed fact—the origin of a tumour-cell, or of a normal tissue-cell from emigrated leucocytes has been imagined but not seen, and although the idea may be true, these facts have not yet been verified.

Quinine exercises a remarkable influence upon the movements of leucocytes; applied in dilute solution ($\frac{1}{1000}$) to a slide of newt's blood, the amœboid movements of leucocytes are arrested; applied locally to a frog's mesentery, or injected into the blood-vessels, it arrests emigration of leucocytes.

Hæmoglobin—its compounds and derivatives.—Reference has been made to the two states of hæmoglobin in the blood, viz. oxyhæmoglobin and reduced hæmoglobin. These are its normal physiological states. Hæmoglobin may, by accident or by experiment, be made to enter into two other combinations—with carbon monoxide, forming carboxyhæmoglobin (COHb), and with nitric oxide, forming nitroxyhæmoglobin (NOHb).[1] Both these combinations are more stable than oxy-hæmoglobin; oxygen is easily separated from hæmoglobin, carbon monoxide is separated with greater difficulty, nitric oxide with still greater difficulty. By passing a current of carbon monoxide through a solution of oxyhæmoglobin, oxygen is quickly and easily displaced, and carbon monoxide takes its place volume for volume in combination with hæmoglobin. By passing a current of nitric oxide through a solution of carboxyhæmoglobin (in the absence of oxygen),[2] carbonic oxide is expelled, and the combination nitroxyhæmoglobin formed. Hæmoglobin is a crystalline body, but although crystalline it is indiffusible; it closely resembles a proteid in chemical constitution, but is peculiar in that its molecule contains iron, in addition to the ordinary proteid constituents C.O.H.N. Hæmoglobin readily absorbs and combines with oxygen; at normal atmospheric pressure 1 gramme Hb absorbs 1·7 c.c. oxygen.

---

[1] The symbols used for hæmoglobin and its compounds—Hb, O_2Hb, COHB, NOHb—are only abbreviations, and not chemical formulæ.

[2] Absence of oxygen is necessary because nitric oxide, N_2O_2, in contact with oxygen becomes N_2O_4, which in contact with water becomes HNO_3 and decomposes hæmoglobin.

Crystals of hæmoglobin are not obtained with the same facility from all animals, nor is their shape the same. They are easily obtained from the rat, mouse, guinea-pig, and squirrel, less easily from dog and man, horse and sheep: from frog's blood they are obtained with great difficulty.

To obtain crystals of hæmoglobin the blood is 'laked' by treatment with water or with chloroform, or, by alternate freezing and thawing, the hæmoglobin is made to pass into solution; the solution yields crystals as it evaporates.

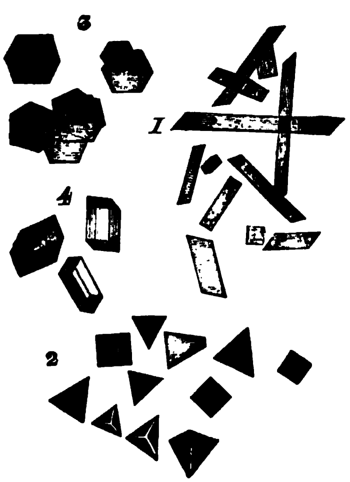


FIG. 10. -HÆMOGLOBIN CRYSTALS.

1. Man or rat. 2. Guinea-pig. 3. Squirrel. 4. Hamster.—Quain's 'Anatomy.'

Carboxyhæmoglobin may be formed accidentally as well as experimentally. Common coal gas contains nearly 10 per cent. of carbon monoxide; the imperfect combustion of charcoal is attended with an abundant production of carbon monoxide, and the respiration of an atmosphere charged with carbon monoxide in either of these ways may be fatal to life, carbon monoxide taking the place of oxygen in combination with hæmoglobin, and annulling its respiratory function. The comparative stability of the compound renders this mode of poisoning all the more dangerous, and decreases the chance of recovery; still, it is important to remember that by the prolonged passage of oxygen through a solution of carboxyhæmoglobin the oxidised state can be recovered, so that in the case of a person whose blood has been more or less profoundly poisoned, artificial respiration should be vigorously persevered in. On the other hand the stability of the compound facilitates the recognition, in doubtful cases, of the cause of death. A stream of CO, or of coal-gas passed through the blood, or through a solution of hæmoglobin, gives a bright red colour, which is not altered by reducing agents, while the colour of oxygenated blood is markedly altered by such agents. In addition to the colour test, the spectroscopic test gives the clearest possible evidence.

The spectrum of carboxyhæmoglobin, or of the blood of a person poisoned by inhalation of carbonic oxide, is hardly distinguishable from that of O_2Hb, even when both spectra are simultaneously observed close above each other. But the addition of a reducing agent, such as ammonium sulphide, at once establishes the difference. Oxyhæmoglobin is reduced, and its two-banded spectrum disappears, being replaced by the single-banded spectrum of reduced hæmoglobin.

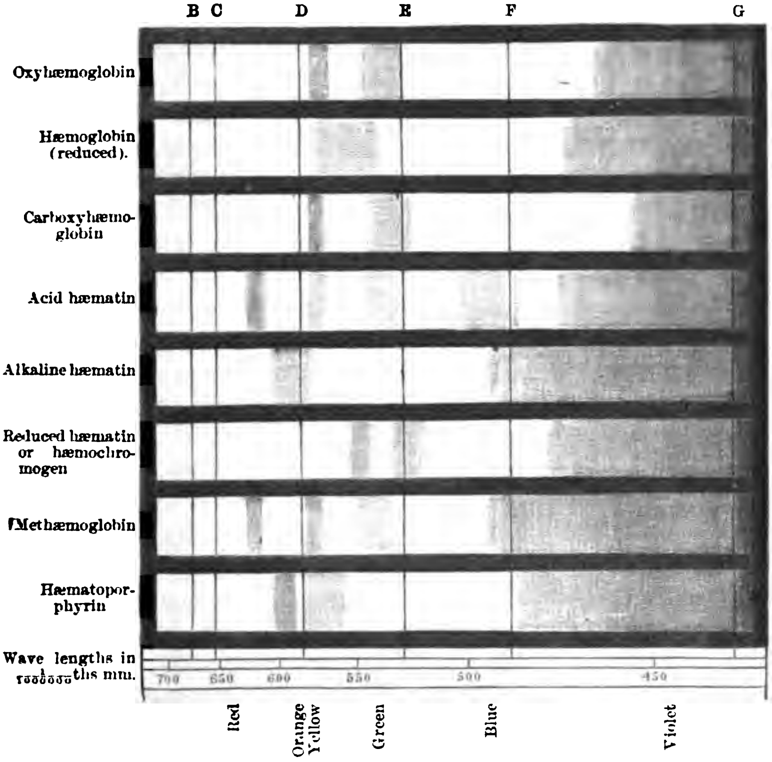


Fig. 11.—Blood Spectra.

On shaking the solution with air, re-oxygenation takes place, and the two-banded spectrum reappears; the latter soon disappears again if the solution is left standing, and the reducing agent has been added in excess. Carboxyhæmoglobin suffers no such change on the addition of reducing agents; its two-banded spectrum remains unaltered.

If blood be left for a few hours at 40° temperature, in contact with a little yeast, its oxyhæmoglobin will be reduced. Its spectrum will be that of reduced Hb. If blood be subjected to a vacuum its gases will disengage themselves, and its oxyhæmoglobin will be reduced.

If arterial blood be left to itself in a well-stoppered bottle it will darken in colour, and become reduced before the occurrence of decomposition. Blood removed from the body does not die at once, nor is it wholly dead even after coagulation has taken place. As it continues to live, so it continues to consume oxygen, and, preserved from contact with the air, it consumes its own oxygen. If blood decomposes, it blackens and becomes reduced; organisms which require oxygen grow and multiply, and remove oxygen from the blood. One kilo of fresh blood will consume about 30 c.c. of oxygen per hour, as compared with one kilo of freshly excised muscle, which consumes about 300 c.c. in the same space of time.

If, during life, arterial and venous blood be removed without bringing them in contact with air, and examined by the spectroscope, both will show the two-banded spectrum of oxyhæmoglobin. If immediately after death arterial and venous blood—*e.g.* from the aorta and from the right auricle—be similarly examined, the former will show the two-banded spectrum of oxyhæmoglobin, the latter the one-banded spectrum of reduced hæmoglobin. The tissues continue to live for some time after an animal has ceased to move and appears dead; internal respiration by the tissues having continued after external respiration in the lungs has ceased, venous blood has become completely reduced, and is found so in the right auricle.

It is possible to observe the reduction of oxyhæmoglobin by the living tissues of the human body. If sunlight be reflected from a finger-nail where it is pink with blood, the two-banded spectrum of O_2Hb will be visible. If a ligature be tied round the finger so as to obstruct its blood-supply, the O_2Hb spectrum will vanish, and under very favourable circumstances the dim band of reduced Hb will become visible.

Of the *derivatives* of hæmoglobin, bodies which are produced by its decomposition, some are normally formed in the human body, others occur abnormally in the body, others again can only be artificially produced out of the body.

The normal derivatives are the *bile and urine pigments*. The abnormal derivatives are *hæmatoidin*, *methæmoglobin*, and *hæmatin*, The artificial derivatives are *hæmochromogen*, *hæmatoporphyrin*, and *hæmin*: methæmoglobin and hæmatin can also be artificially produced from hæmoglobin.

With regard to the natural derivatives little is known beyond the fact, that the pigments of the bile and of urine (bilirubin, urobilin) are derived from hæmoglobin. *Hæmatoidin* is a crystalline substance found in old blood-clots in the brain and other organs; it is evidently derived from hæmoglobin, but it does not contain iron, and it gives the same reactions as *bilirubin*, with which it is therefore regarded as identical. Hæmatoidin thus furnishes accidental evidence of the derivation of bilirubin from hæmoglobin. *Methæmoglobin* and *hæmatin* are met with in pathological products—in 'smoky' urine, *i.e.* urine containing blood which has transuded from the kidney—and in 'coffee-ground' vomit, *i.e.* more or less digested blood from bleeding vessels in the stomach. Methæmoglobin is simply a modified kind of oxyhæmoglobin; hæmatin is one of the products of the decomposition of hæmoglobin. The two bodies give very similar spectra, but may, however, be easily distinguished by the effects of a reducing agent, such as ammonium sulphide: the spectrum of methæmoglobin becomes altered and gives place to that of reduced hæmoglobin, which when the fluid is aërated by shaking, is replaced by the spectrum of oxyhæmoglobin; the spectrum of hæmatin is also altered by the reducing agent, and gives place to that of reduced hæmatin, on re-oxygenation the spectrum of hæmatin reappears. Thus the chief distinction between the spectra of the two bodies is that from methæmoglobin the spectrum of oxyhæmoglobin can be recovered, while from hæmatin it cannot. The blood of animals which have been poisoned by inhalation of nitrite of amyl has a peculiar chocolate-brown colour, and gives the spectrum of methæmoglobin. Both these bodies may also be classed as artificial derivatives, although, perhaps, methæmoglobin should be regarded as modified oxyhæmoglobin rather than as a decomposition-product. By adding acetic acid to diluted blood, the hæmoglobin is decomposed into hæmatin and a proteid; by shaking this fluid with ether a coloured ethereal solution is obtained, which gives the spectrum of *hæmatin in acid solution*. On rendering this fluid alkaline by the addition of caustic potash in excess, the spectrum is altered to that of *hæmatin in alkaline solution*. On adding a reducing agent to the alkaline solution the spectrum is altered to that of reduced hæmatin. If the blood be decomposed by caustic potash in the absence of oxygen, a body called *hæmochromogen* is produced, which is identical with reduced hæmatin, giving the same spectrum, and as soon as it comes in contact with air, giving the spectrum of hæmatin. Hæmatin contains all the iron of hæmoglobin; if, however, hæmoglobin be decomposed by still more powerful means than above mentioned—by strong sulphuric acid, or by heating with fuming hydrochloric acid—a more profound decomposition is effected, and as the result a body called *hæmatoporphyrin* is obtained, the iron being separated by the acid in the form of ferrous sulphate or chloride.

Hæmin is a compound of hæmatin with hydrochloric acid. It is a crystalline body of great importance in medico-legal practice, as it furnishes a most reliable test of the nature of stains supposed to be of blood. By boiling on a slip of glass a little dry blood with glacial acetic acid and a minute fragment of sodium chloride, this compound is formed, and can easily be recognised under the microscope as small brown rhombic crystals. They are commonly spoken of as Teichmann's crystals.

We have learned that hæmoglobin can combine with O_2 and with CO in or out of the body; that in the body it may decompose and give rise to hæmatin or to the iron-free body hæmatoidin or bilirubin; that analogous changes can be brought about outside the body by the action of reagents, hæmatin being produced by comparatively weak reagents, and an iron-free body, hæmatoporphyrin, by strong acids. Methæmoglobin is so little removed from oxyhæmoglobin as hardly to deserve a place among derivatives; it is produced by the weakest reagents and it can be easily restored to the original state as oxyhæmoglobin. It is to b remembered that in the contents of the stomach and of th urinary bladder, blood-pigment may be found, in the form o oxyhæmoglobin or of methæmoglobin or of hæmatin.

Estimation of hæmoglobin.—If one c.c. of normal blood an one c.c. of 'poor' blood be each diluted with 100 c.c. of water and the two solutions compared, that of normal blood will b evidently of a deeper tint than that of 'poor' blood, *i.e.* th latter evidently contains less hæmoglobin. If instead of addin at once 100 c.c. of water to the 1 c.c. of poor blood, the wate is added gradually until the tint is judged to be equal to th of the diluted normal blood, then from the quantity of wate added we may estimate how much hæmoglobin is present in th poor blood as compared with normal blood. For instance, equality of tint being established with 20 c.c., the hæmoglobin value is $\frac{20}{100}$ of the normal; if with 30 c.c it is $\frac{30}{100}$ of the normal. In the practical application of the method, smaller quantities of blood are taken, *i.e.* $\frac{1}{50}$ c.c.=20 cubic mm., and this is diluted until it is equal in tint to a permanent standard colour made with glycerine and carmine, and equivalent to normal blood diluted 100 times. Thus arranged the apparatus is termed a *hæmoglobinometer.* If the 20 cubic millimeters of blood give equality of tint with 2 cubic centimeters, *i.e.* 2,000 cubic millimeters of water, the amount of hæmoglobin is normal; if with 1,000 the amount is half normal; if with 500 the amount is one-quarter normal.

A more convenient instrument to fulfil the same purpose consists of a glass cell in which the tint of diluted blood is compared with that of a wedge of ruby glass ; the wedge can be slipped to and fro so as to bring a thinner or a thicker portion into view, so giving a paler or a deeper tint for comparison with the blood ; the sliding wedge is graduated so as to indicate percentage of hæmoglobin (von Fleischl).

Identification of spectra,—preparation of suitable solutions.—The various spectra above described may at first sight appear to be somewhat difficult of identification, and it will, therefore, not be amiss to indicate their salient points of distinction.

Of the eight spectra given, four possess *two* characteristic absorption bands, and four possess *one* characteristic absorption band. Two of these, *i.e.* methæmoglobin and acid hæmatin, have accessory bands, indicated by light shading in Fig. 11, but omitted in Fig. 12.

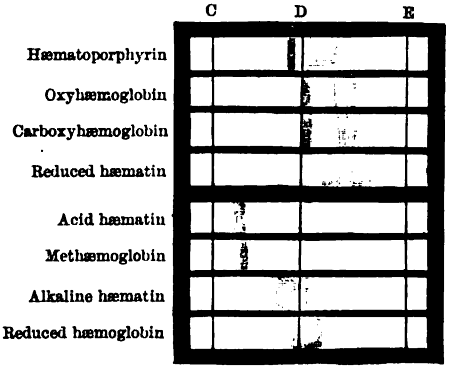


FIG. 12.

A double spectroscope should be used, in which two spectra, one above the other, can be simultaneously observed, and the requisite substances may be readily prepared and identified as follows, using a solution of 1 part blood in 9 parts water, and looking through a layer one centimeter thick.

1. *Oxyhæmoglobin.*—Dilute the above solution.

2. *Hæmatoporphyrin.*—Add blood drop by drop to strong H_2SO_4.

Compare these two spectra one above the other; the bands o hæmatoporphyrin are obviously nearer the red end of the spectroscop than those of the O_2Hb.

3. *Carboxy-hæmoglobin.*—Pass coal-gas through the solution blood (1 in 100) and compare one above the other the spectra of O_2H and COHb; the bands of COHb are slightly nearer the violet end.

To each add a few drops of ammonium sulphide. The spectru of O_2Hb gives place to that of reduced Hb, that of COHb persis unaltered.

4. *Methæmoglobin.*—Add a few drops of amyl nitrite to the dilu solution of Hb. Notice that the colour changes from pink to brow and that a new band makes its appearance between C and D. This the characteristic band by which methæmoglobin is identified.

5. *Acid Hæmatin.*—Take equal parts of acetic acid and ether in test-tube and gradually drop into it diluted blood (as above, 1 in 1 The layer of ether takes acid hæmatin into solution; the characterist band of its spectrum is between C and D, in the same position as th of methæmoglobin. The two bodies are distinguished by the effect a reducing agent (ammonium sulphide), which causes the methæm globin spectrum to give place to that of reduced hæmoglobin, and t acid hæmatin spectrum to give place to that of reduced hæmatin (t acid hæmatin solution should be rendered alkaline before adding t reducing agent).

6. *Alkaline hæmatin.*—Into a solution of caustic potash in absol alcohol drop dilute blood (1 in 10). The characteristic band of t spectrum is towards the red side of D. On examination of the spec of acid and of alkaline hæmatin one above the other, it will be s that the prominent band of acid hæmatin is on the red side of alkaline hæmatin band. The addition of a reducing agent to alkal hæmatin causes the two-banded spectrum of reduced hæmatin to appe

7. Compare, one above the other, the spectra of alkaline hæma and that of reduced hæmoglobin, and notice that the hæmatin ban on the red side of the hæmoglobin band.

8. Compare the spectra of reduced hæmatin and of oxyhæmoglo and notice that the two bands of oxyhæmoglobin are on the red of the two bands of reduced hæmatin.

Tests for blood.—It is often required to determine whet or no a pathological fluid contains blood—whether or no a st on weapons or clothes is due to blood. We have four tests which blood may be identified. (1) By the microscope we determine the presence or absence of blood-corpuscles in a f or in a fresh stain. We may be able to determine whether blood is mammalian or that of a bird or fish, but we cannot specify what kind of mammalian animal is the source of the blood under examination. There are, it is true, differences of size between the red corpuscles of various mammalia (*vide* fig. 3), and we might thus, for instance, be able to deny that a stain caused by goat's blood was caused by human blood, but we should not be able in practice to distinguish human blood from that of animals such as the cat, dog, rabbit, ox, &c. On the other hand we might positively distinguish the blood of fowl or fish from that of mammalia. A knife stained with blood containing oval corpuscles has, in all probability, not served to kill a man; a girl supposed to spit blood which is found to contain oval blood-corpuscles, has probably obtained it from a fowl, and is certainly attempting to mislead.

In many cases corpuscles may not be found and yet blood be present; it will, however, be identified by other tests, which, indeed, are in all cases to be employed as confirmatory tests. Of these the best is (2) *the hæmin test*, applied as above stated; the presence of hæmin crystals proves the presence of blood, but gives no information as to its kind; any kind of blood can yield hæmin crystals, and a blood-stain, however old, will yield them.

(3) The *spectroscope* affords a convenient and expeditious means of ascertaining whether or no a coloured fluid owes its colour to blood. The fluid may contain hæmoglobin or its derivatives. An ordinary blood-stain dissolved in water gives the oxyhæmoglobin spectrum, or, if old, it may give the methæmoglobin or hæmatin spectrum: the blood of a person poisoned by coal-gas will give the carboxyhæmoglobin spectrum: blood in the urine, or in the vomited contents of the stomach, may give either the oxyhæmoglobin, the methæmoglobin, or the hæmatin spectrum. These will be distinguished as above described and by the alterations effected by reducing agents. It is of practical importance to remember that the spectrum of oxygenated hæmatin is much less distinct than that of reduced hæmatin; so much so that a pathological fluid containing hæmatin may yield a blank spectrum until after the addition of ammonium sulphide. It is also to be borne in mind that the hurried examination of a pink fluid and the discovery of a two-banded spectrum is not proof positive that hæmoglobin is the colouring agent, for carmine gives a very similar spectrum. If a very small quantity of fluid is available, the spectroscope is used in

combination with a microscope, being substituted for the eyepiece of the latter: an instrument of this kind is termed a *microspectroscope.*

(4) On the addition of fresh tincture of *guaiacum and ozonic ether* (which contains hydrogen peroxide) to a fluid which contains a trace of blood, a sapphire-blue colour is produced. The test is, however, not characteristic, for blood is not the only substance by which the colour is elicited.

The composition of plasma, lymph, chyle, and serous fluids Coagulation. Facts and theories.—The proteids of blood are fo the most part contained in the plasma, the corpuscles containing a comparatively small quantity of proteid (paraglobulin), though their chief constituent, hæmoglobin, has an elementary composition closely resembling that of proteids, and yields proteid (globin) when it is decomposed by heat or by acids. The proteids of the *plasma* are fibrinogen, paraglobulin, and serum-albumin the two last are in about equal, but somewhat variable proportion, and amount to nearly 10 per cent. of the liquid fibrinogen is present in very small amount, only about ·2 to · per cent. *Serum* differs from plasma in that it contains n fibrinogen; it contains paraglobulin and serum-albumin in th same proportion as does the plasma. Thus it appears that thes fluids are, above all, highly albuminous solutions, containin nearly as much proteid as is contained in ordinary white egg, which consists of ten to twelve per cent. of albumin. Norma *lymph* is essentially a dilute plasma; it is, like it, a coagulabl albuminous solution, with roughly 5 per cent. of proteids, namely fibrinogen, paraglobulin, and serum-albumin. *Chyle* is lymph plus fat, and its composition differs with the state of digestion chyle taken from an animal in full digestion of fat has bee found to contain as much as 15 per cent. of fat, *i.e.* three time as much as is contained in ordinary milk. All the above-name fluids, with the exception of serum, are spontaneously coagulable plasma yields the firmest and most abundant clot, it is, in fac a blood-clot minus the red corpuscles, and the fluid in whic the clot floats is serum; lymph, being a more dilute fluid, yiel a less considerable clot, and chyle yields a soft white clot li a loose curd.

Abnormal lymph, such as gathers in serous sacs, constituti *serous effusions* (pericardial, pleuritic, peritoneal and hydroce fluids), varies as regards its proteids and as regards its coagul bility. All serous effusions contain proteids (serum-albumin and serum-globulin) in proportions varying between ·5 and 5 per cent. Some serous effusions coagulate spontaneously; others only after addition of serum or of fibrin-ferment; others again are quite uncoagulable. An effusion of the first kind amounts practically to a dilute lymph, and contains in addition to the serum-proteids, fibrinogen, fibrin-ferment, and a considerable number of leucocytes: an effusion of this kind has usually formed rapidly in consequence of an acute inflammation of a serous membrane. Effusions of the third kind amount practically to a dilute serum; they are usually chronic, and contain only a small proportion of proteids with little or no fibrinogen and no ferment. Effusions of the second class are intermediate between the two extremes; they contain fibrinogen as well as the two serum-proteids, but no fibrin-ferment; they do not coagulate spontaneously, but only after the addition of blood-serum or shreds of fibrin—in short, of any substance containing fibrin-ferment. The relations which these effusions bear to plasma and lymph on the one hand, and to serum on the other, are exhibited in the following table:—

Plasma and Lymph	Serous effusions			Serum
Coagulable	I. Coagulable	II. Coagulable by ferment	III. Uncoagulable	Uncoagulable
Serum-albumin	Serum-albumin	Serum-albumin	Serum-albumin	Serum-albumin
Serum-globulin	Serum-globulin	Serum-globulin	Serum-globulin	Serum-globulin
Fibrinogen	Fibrinogen	Fibrinogen	—	—
Fibrin-ferment	Fibrin-ferment	—	—	Fibrin-ferment

It is with the second variety of serous effusion—usually pericardial fluid or the fluid of hydrocele—that certain classical experiments have been made bearing upon the theory of coagulation. Buchanan, in 1831, and Alexander Schmidt, in 1861, observed that such a serous fluid—*e.g.* hydrocele fluid—uncoagulable by itself, yielded a clot if mixed with serum and left to stand.

It was supposed by Buchanan that a substance dissolved in the serum effected the transformation into fibrin of a substance dissolved in the hydrocele or other fluid. He found that the same transformation could be effected by washed blood-clot, by portions of buffy coat, &c., and that the efficiency and rapidity of clotting was proportionate to the quantity of white corpuscles present. From which he concluded that the transforming agent was derived from the white corpuscles, and he compared its action to that of rennet upon milk. Translated into modern language, Buchanan's explanation of the experiment would run thus: a *ferment* dissolved in serum and derived from the leucocytes effects the transformation into fibrin of *fibrinogen* dissolved in the hydrocele or other fluid. In the experiments above described, the two fibrin factors are separately present each in one of two liquids which give a clot when they are mixed; in the case of the blood or blood-plasma, both factors are present in the plasma, and the blood or blood-plasma is of itself coagulable. As we shall see, this is the generally accepted theory of the present day.

A. Schmidt separated and named the proteids of these various fluids; from hydrocele fluid he separated the fibrin antecedent, and gave to it its name fibrinogen; he found that the fluid after separation of fibrinogen was no longer coagulable with serum, while the separated fibrinogen dissolved in saline solution, and, mixed with serum, might coagulate; from serum he separated a body which he named fibrinoplastin (=paraglobulin),[1] and found that a solution of this body acts upon hydrocele fluid, or fibrinogen solution, in the same manner as serum. But he found that it was possible for these two bodies to be present together in the same liquid, *e.g.* hydrocele fluid, which does not coagulate until serum is added. He concluded that serum contains a ferment derived from the leucocytes, and that the union of fibrinogen and paraglobulin was brought about by the presence of this ferment. Schmidt's theory assigns the fibrin-formation in coagulation to three fibrin-factors: (*a*) fibrinogen, (*b*) paraglobulin, (*c*) fibrin ferment.

The researches of Hammarsten have, however, proved that paraglobulin is not an indispensable factor in coagulation: we are thus brought back to the view that coagulation depends upon the conversion into fibrin of a single body (fibrinogen) under the influence of a ferment (fibrin-ferment) which is derived from the leucocytes. Paraglobulin plays only an accessory part in the process, its presence leads to a more decided and abundant formation of fibrin, an influence which is possessed by many other bodies—by casein, by calcium chloride, and by nitrogenous derivatives of the proteids, such as lecithin (Wooldridge), glycin, leucin, tyrosin, &c.

---

[1] 'Paraglobulin' and 'serum-globulin' are synonymous terms, denoting the same body as 'fibrinoplastin.' This last term has however fallen out of use.

Methods of separating the proteids of plasma and of serum.—*Fibrinogen* may be prepared from plasma, or from pericardial or hydrocele fluid, and the best method is that known as the sodium chloride method (Hammarsten). Magnesium sulphate plasma (blood $\frac{2}{3}$, magnesium sulphate saturated solution $\frac{1}{3}$, centrifuged) is treated with an equal volume of saturated solution of NaCl (containing about 26 per cent.). A precipitate forms, which is separated and well washed with a semi-saturated solution of NaCl (about 13 per cent.). The precipitate is then dissolved in a quarter saturated NaCl solution (about 6 per cent.). To this solution, after filtration, is added an equal bulk of saturated NaCl solution, the percentage of NaCl in the mixture being now about 16 per cent., by which the precipitate is reproduced. The precipitate may be purified further by redissolving in NaCl 6 per cent., and reprecipitating with saturated NaCl solution, and at the end of these operations it consists solely of fibrinogen. The method depends upon the comparative solubilities of fibrinogen and of paraglobulin in solutions of NaCl of various degrees of concentration, and the object attained by the steps above described is the gradual and complete separation of the two bodies.

Both are soluble in NaCl solution between 5 and 8 per cent. Fibrinogen is precipitated when the solution of NaCl is between 12 and 16 per cent. Paraglobulin is not precipitated in sensible quantity until the solution of NaCl is above 20 per cent. The first precipitate consists of fibrinogen with an admixture of paraglobulin; at the end of the process only fibrinogen is left.

The same method is applicable to other liquids, such as hydrocele or pericardial fluids, and is the best means of obtaining fibrinogen from them when they contain it; this, however, as has been mentioned above, is not invariably the case.

Paraglobulin or *serum-globulin* is best prepared from serum. Saturation with sodium chloride (Hammarsten), or prolonged dialysis (A. Schmidt), or careful neutralisation with dilute acetic acid (Panum), or the prolonged passage of CO_2 through dilute serum (A. Schmidt), or semi-saturation with ammonium sulphate, all cause a more or less complete precipitation of paraglobulin from serum. Saturation with magnesium sulphate is however the most approved method, and gives a complete precipitation of paraglobulin (Hammarsten). To estimate the amount of globulin present, the fluid must be completely saturated with $MgSO_4$, and to this end it is necessary to subject it to prolonged agitation with an excess of the salt. The precipitate is then collected on a filter, washed with saturated $MgSO_4$ solution, dried at 100°, washed with boiling water, and finally dried and weighed.

To prepare *fibrin-ferment*, serum is mixed with twenty times its bulk of alcohol, and allowed to stand for several weeks; the proteids are thereby coagulated and form a deposit at the bottom of the flask. The alcohol is poured off and the residue extracted with water and filtered. The filtrate contains very little proteid, but possesses the same property of promoting the coagulation of, *e.g.* hydrocele fluid, which is possessed by 'washed clot' or fibrin or serum, *i.e.* it contains fibrin-ferment in solution (A. Schmidt). This ferment has not, however, been isolated as a solid substance.

It is probably of the nature of, or closely associated with a globulin, for if serum is separated by precipitation with magnesium sulphate into (*a*) globulin and (*b*) serum minus globulin, it is found that ferment action is possessed by a solution of th separated globulin, and not by the residual serum (Halliburton)

Blood received into alcohol directly from an artery, and th residue subsequently extracted with water, yields a solution possessing the properties of fibrin-ferment, though in much les degree than a solution prepared from serum or from blood whic has been shed some time. This may be accepted as evidenc that the ferment is normally present in small proportion in circulating blood (A. Schmidt).

Serum-albumin is obtained as follows: paraglobulin is precipitated by the complete saturation of serum with $MgSO_4$; th filtrate, which now contains only serum albumin, is dialysed f twenty-four hours or more in order to remove the magnesiu sulphate; the solution is evaporated *in vacuo* over sulphur acid, or in a shallow vessel at a temperature not exceeding 40 Serum-albumin is thus obtained as a yellowish, brittle soli (Hammarsten).

The points by which solutions of fibrinogen and of par globulin are distinguished are (1) the influence of fibrin-fermen (2) the effect of semi-saturation by NaCl, and (3) their temper ture of coagulation. Fibrinogen comes down at 56° C., par globulin at 70° to 75°. Serum-albumin solutions coagula between 70° and 85° according to their acidity and concentratio

Influence of the vessels upon coagulability.—Normally the blood remains fluid while it is within the vessels, and coagulates shortly after it is shed. Abnormally it may coagulate in the vessels, or it may fail to coagulate after removal from them.

1. *Normally the blood remains fluid while in the vessels.*—The production of fibrin-ferment from leucocytes probably takes place continually though slowly, in circulating as well as in shed blood, and it is moreover probable that this fibrin-ferment is somehow disposed of and removed by the living vessels as fast as it is formed. This may be regarded as an explanation of the non-coagulation of blood under normal circumstances, and certain facts may be adduced to illustrate this presumed action of living vessels.

A jugular vein full of blood tied in two places and cut out of the body, keeps the blood fluid for hours; the same thing may be done with a turtle's or frog's heart. If the blood be allowed to escape an hour or two after the vessel has been excised, it forthwith coagulates, but if it be left in the vessel it may remain fluid indefinitely and begin to decompose. That this restraining action of the vessels is peculiar to intact tissue, is indicated by the fact that in the body, blood which escapes from a broken vessel forms clots, although it is in contact with living tissues. Serous effusions (of the first class alluded to above) are likewise kept fluid by the influence of the living membrane enclosing them; the pericardial fluid of the horse, for instance, coagulates spontaneously if it is removed immediately after death, but does not do so if it is left for a few hours undisturbed in the pericardium; this is probably due to a destruction of ferment by the influence of the still living membrane.

2. *Abnormally the blood may coagulate in the vessels.*—The blood is liable to coagulate in an injured or diseased vessel ('thrombosis'), and it sometimes happens that the blood coagulates *en masse* in a large area of uninjured vessels—in the pulmonary or in the portal vessels, for instance—causing sudden death by complete arrest of the circulation. The local coagulation is brought about by the gradual deposition of fibrin upon the roughened or irregular internal surface of a vessel, preceded and, in all probability, caused by an accumulation of leucocytes and of blood-platelets, which adhere to the rough surface and disintegrate; the resulting clot is called a 'thrombus.' The more general coagulation is probably due to an ex-

cessive production of fibrin-ferment; it may be experimentally effected by the injection of putrid matter, or of hæmoglobin, or of distilled water (Schmidt), or of extracts of the thyroid gland and of the testis (Wooldridge). It is one of the dangers attendant upon transfusion.

3. *Abnormally the blood may fail to coagulate after removal from the vessels.* Peptones—or, more accurately speaking, albumoses—injected in suitable quantity into the blood-vessels of a dog (·3 gramme per one kilogramme body-weight), rapidly disappear, but leave a remarkable alteration of the blood, viz. a greatly diminished coagulability; blood taken from the animal directly or within an hour after injection fails to coagulate, although now all peptone has disappeared. Little by little coagulability is restored; blood drawn on the following day coagulates normally. It is to be observed that the effects entirely fail on the rabbit, and are not so well marked on cats as they are on dogs. The abolition of coagulability is associated with a considerable fall of blood-pressure due to dilatation of the splanchnic vessels. It is probable that a deficiency of fibrin-ferment in peptone-blood is in part accountable for the non coagulation; the leucocytes of normal blood rapidly break up in large numbers and yield abundant fibrin-ferment; the leucocytes of peptone-blood remain unchanged, and fibrin-ferment is no liberated. These effects of peptone are only brought about on blood while it is in the body; the peptone vanishes in a few minutes, and the defective coagulability persists for a few hours but peptone added to freshly drawn blood does not disappear and coagulation, though somewhat retarded, is not wholly prevented. On the other hand the addition of fibrin-ferment, or o decomposing albumen, causes peptone-blood to coagulate; it may also coagulate when decomposition sets in. Similar effects o circulating blood have been produced by the injection of leech extract, and the coagulation of freshly drawn blood can b arrested by leech-extract (Haycraft), which owes this propert to the presence of an albumose (Dickinson).

Blood made to pass repeatedly through the heart and lungs and kept away from the systemic circuit, gradually loses it coagulability (Ludwig and Pawlow). Blood received in a vesse of oil, or smeared with oil, is thus preserved from contact wit foreign bodies, and coagulates slowly, or partially, or not at all.

CHAPTER III

THE CIRCULATION

PAGE

42 **General principles**: Course of the blood—Systemic vessels—Pulmonary vessels—Valves—Rhythm of the heart's action—Cardiac cycle—Systole and diastole—Blood-pressure—Nervous mechanism.

45 **Physiological anatomy of the heart**: Inflamed pericardium—Pericardial friction—Pericardial effusion—Relation between bulk and work—Hypertrophy—Structure of the frog's heart.

48 Examination of the human heart—Percussion—Auscultation—The cardiograph—Duration of systole and of diastole.

55 **Blood-pressure**: In the arteries—The factors of blood-pressure—The manometer—'Tension'—Variations of blood-pressure and of blood-flow—Local and general variations—Effects of addition and removal of blood—Blood-pressure in the capillaries, in the veins, and in the heart—Influence of varying arterial pressure upon venous and upon pulmonary pressure.

65 * **Further physical considerations**: Velocity and pressure—Instruments used—Stromuhr—Tachometer—Dromometer—The time of circulation—The capacity of the ventricles—The work of the heart—Elasticity curves of blood-vessels—The plethysmograph—The oncometer—The sphygmomanometer.

79 **The pulse**: Frequency—Conditions of increased frequency—Conditions of diminished frequency—Large pulse, small pulse—Strong pulse, weak pulse—Hard pulse, soft pulse—Long pulse, short pulse—Slow pulse, quick pulse—'Rapid' and 'slow' pulses—Dicrotic pulse—Intermittent pulse—Irregular pulse—Venous pulse—Capillary pulse—The *Sphygmograph*: Marey's instrument—Its value—The normal pulse-tracing—High-tension pulse—Low-tension pulse—Nature of the dicrotic wave—Velocity of the pulse.

87 ***On the properties and mode of contraction of cardiac muscle**: Excised heart—Ventricle-apex—Ventricle-strip—The coronary arteries—Stannius' experiments—1st ligature—2nd ligature—Experiments on stanniused hearts—'All or nothing'—The staircase—The refractory period—Tetanus?—The wave of contraction—'Blocking.'

93 * **Drugs by which the action and properties of the heart can be modified**: Muscarin—Pilocarpin—Atropin—Antagonism of muscarin by atropin—Nicotine—Physostigmine—Curare—Digitaline—Veratrine—Aconitine—Alcohol—Chloroform and ether—Neutral salts—Nutritive fluids.

98 * **Influence of the nervous system upon the heart, and upon the blood-vessels**: Physiological anatomy of cardiac nerves—Physiological anatomy of vaso-motor nerves.

101 **The vagus**: Effect of division and of excitation—Inhibition—Latent period and duration of vagus action—After-effects—Successive stimulation of both vagi—The spinal accessory—Inhibition on man—Action of vagus *post mortem*—Reflex inhibition—Fainting—Expiratory slowing—Swallowing—'The trophic' theory—*The accelerator nerves.*

106 **Vaso-motor nerves**: Constrictors and dilatators—Cervical sympathetic of rabbit, and chorda tympani of dog—Nerves of the limbs—The splanchnic nerves—Nervi erigentes—Muscular nerves—The dog's mouth—The *vaso-motor centre*: Destruction and excitation of spinal bulb—*The 'depressor' nerve*: Exceptional effects—Local vaso-motor reflexes.

113 **The lymphatic circulation**: Lymph-hearts—Lymphatic glands.

General Principles.—The blood does not remain stagnant, it circulates. From the heart it is driven into the arteries, from the arteries into the capillaries, from the capillaries into the veins, from the veins finally it returns into the heart. The heart of mammalia is a double organ, and each part of this double organ is composed of two chambers—one auricle and one ventricle; thus the entire organ comprises four chambers, viz., the left auricle, the right auricle, the left ventricle, the right ventricle. The arteries lead from the ventricles, the aorta o systemic artery from the left, and the pulmonary artery fron the right. The veins lead to the auricles—the venæ cavæ, o systemic veins to the right, and the pulmonary veins to th left. Outside the heart the blood flows from ventricle to auricl through arteries, capillaries, and veins; inside the heart th blood flows from auricle to ventricle. A drop of blood wi complete its circulation, passing through the several chambers c the heart and through the vessels in the following order:—le auricle, left ventricle, systemic arteries, systemic capillarie

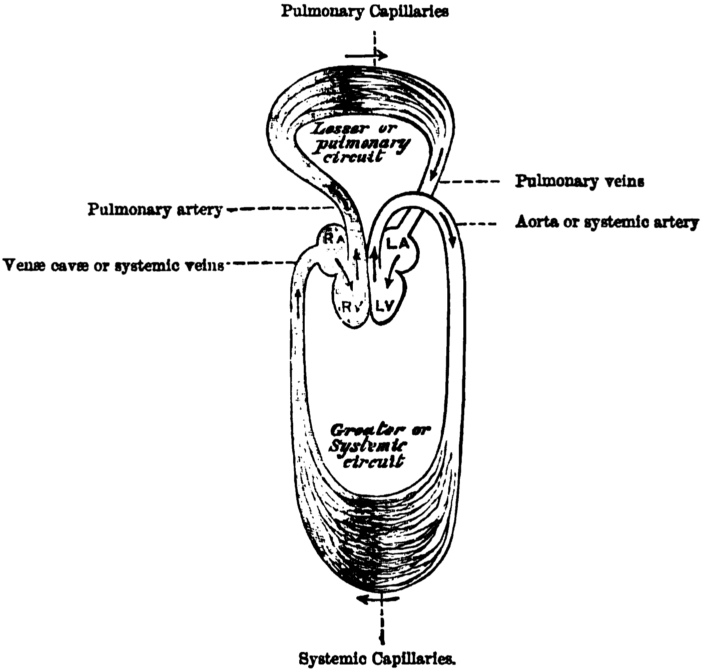


Fig. 13.—Diagram of the Circulation.

systemic veins, right auricle, right ventricle, pulmonary arteries, pulmonary capillaries, pulmonary veins, left auricle; thus a drop of blood, to complete its circulation, makes two journeys from and to the heart—one through the systemic arteries, capillaries, and veins, from the left ventricle to the right auricle; the other through the pulmonary arteries, capillaries, and veins, from the right ventricle to the left auricle. The first circuit is called the *systemic* or *greater circuit*; the second is called the *pulmonary* or *lesser circuit.* The first circuit conveys the blood through the whole system to all the tissues of the body; the second circuit conveys the blood through the lungs.

The force by which the blood is made to circulate is supplied by the heart muscle, which by its forcible contraction expels the blood and empties the four chambers in a regularly repeated order. Apart from diseased conditions, the blood is driven in only one direction, namely from auricles to ventricles, and from ventricles to arteries, and is prevented from flowing back in the opposite direction by valves. The *aortic semilunar valves* and the *pulmonary semilunar valves*, at the origin of the aorta and pulmonary artery, prevent reflux of blood from arteries to ventricles, while they offer no obstruction to the passage of blood from ventricles to arteries. The *mitral valves* between left auricle and left ventricle, the *tricuspid valves* between right auricle and right ventricle, prevent reflux of blood from ventricles to auricles, while they offer no obstruction to the passage of blood from auricles to ventricles.

The human heart contracts with regularity at a rate of about seventy per minute, and its parts act in regular sequence, each contraction or active period being succeeded by a passive period, during which the previously contracted chamber is relaxed and becomes refilled with blood. This regular sequence of action and rest is termed the *rhythm*, and is of the following character: a short contraction of the auricles, immediately followed by a somewhat more prolonged contraction of the ventricles, the two auricles contracting together and the two ventricles contracting together. Each cardiac revolution or cycle consists of (1) a short sharp contraction of the two auricles; (2) a longer contraction of the two ventricles; (3) a period of rest during which the heart is becoming refilled. The contraction of any part of the heart is called its *systole*; the opposite state, *i.e.* relaxation, is called its *diastole*; thus auricular systole signifies contraction of auricles, auricular diastole their relaxation; ventricular systole signifies contraction of ventricles, ventricular diastole their relaxation; and when the terms 'systole' and 'diastole' are used alone, or when 'cardiac systole' or 'cardiac diastole' are spoken of, it is the state of the ventricle to which reference is made.

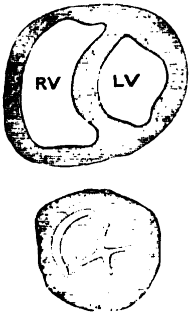


Fig. 14. — Transverse Section through the Middle of the Ventricles of a Dog's Heart in Diastole and in Systole. (After Ludwig.)

Successive beats of the ventricles drive successive charges of blood into the arteries, and produce a *pressure* of blood within them: if an artery be opened the blood spurts from it in jets; if an artery be weakened by disease the pressure of the blood may burst it. There is no opportunity for blood to escape backwards from the arteries to the ventricles during diastole because the semilunar valves are closed; it can only move onwards from aorta to large trunks, thence to branches, and finally to the small twigs called arterioles, and to the minute channels called capillaries. It is through these channels that the distended arterial system is relieved, and it is owing to the *resistance* which these narrow channels offer that the arterial system is distended at all, and a pressure kept up within it. The greater or systemic circuit offers a greater resistance than does the lesser or pulmonary circuit; more force is required to drive the blood through the former than through the latter; parts concerned in driving and carrying blood through the system are more bulky and more robust than parts concerned in conveying blood through the lungs; thus the left ventricle has walls three times as thick as the right ventricle; the aorta and the systemic arteries are much thicker than the pulmonary artery and its branches; the aortic are much coarser and stronger than the pulmonary valves; the mitral curtains and their cords coarser and stronger than the tricuspid. The same difference, but much less pronounced, marks the auricles; the left is somewhat stronger than the right, but not much so; both are thin in comparison with the thinner of the two ventricles, the reason being that the auricles do not have to contract against any great resistance.

Beyond the resistance which is offered by the minute arteries and capillaries, *i.e.* in the veins, the pressure is very low—barely sufficient to send the blood onwards towards the heart—muscular movements, and in particular the movements of respiration, helping to this result; many veins have valves which, while they allow blood to move onwards towards the heart, do not allow it to move backwards towards the capillaries, so that if a vein full of blood is compressed by contracting muscles, its contents are squeezed towards the heart. In the lower extremities this disposition is particularly prominent, and has, as its effect, that the column of venous blood with each muscular movement is pressed upward from valve to valve, as up a ladder.

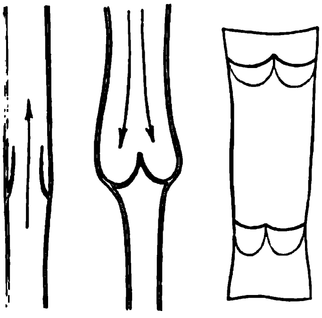


FIG. 15.—VENOUS VALVES. TO RIGHT OF FIG. A VEIN LAID OPEN TO EXPOSE THE POCKET-SHAPED VALVES.

The heart's movements are involuntary, and will even continue for a short time after the heart has been removed from the body; they may be accelerated or retarded through nervous channels; the escape of blood into the capillaries may be facilitated or obstructed by the relaxation or contraction of the muscular fibres which constitute the chief bulk of the walls of the minute arteries —such relaxations and contractions are for the most part effected through nervous channels. Thus the heart and vessels are not set for life to do uniform duty, but can be played upon and modified in action according to the requirements of special circumstances.

The heart.—*Physiological anatomy.*—Our knowledge of the physiology of the heart is based upon the study of the living organ in all classes of animals, but more especially in mammalia, such as the dog, cat, rabbit, horse, and man himself, and in cold-blooded animals such as the frog, toad, and tortoise.

In mammalia the organ is constructed upon the plan above described, viz., it consists of two auricles or ante-chambers leading into two ventricles. It is essentially composed of *muscle* of a peculiar character, and is externally surrounded by a fibrous bag, the *pericardium*, internally lined by a delicate membrane, the *endocardium*. The *pericardium* is disposed in two layers, a visceral and a parietal layer, and these two layers are closely applied to each other, lined by a smooth membrane of endothelium, and barely moistened by serous fluid, so that with the movements of the organ the two surfaces glide upon each other without friction. This is in the healthy state, but when, in consequence of inflammation, the pericardium has become rough, the movements of the heart cause a friction between the two roughened surfaces which may be heard or even felt, and the natural moisture may become exaggerated into a large amount of serous fluid.

The *endocardium* in health is a perfectly smooth membrane, lining the cavities of the heart and covering all its valves. As one of the chief consequences of its inflammation, it may become rough and irregular, so that the valves no longer act properly, and neither allow the blood to pass smoothly in the right direction, nor efficiently prevent its return in the wrong direction. Under such circumstances the natural sounds are obscured or replaced by noises or 'bruits.'

The *muscle* of the heart, as examined under the microscope, differs from all other muscle, and occupies an intermediate position between involuntary or unstriped muscle and voluntary or striped muscle. It is composed of short, four-sided cells with short thick branches, which join with the branches of other cells, thus forming a closely interlacing network; the cells are striated across their length, they possess nuclei deeply embedded in their substance, and they are devoid of any surrounding membrane (sarcolemma).

The *bulk* of muscle bears an evident relation to the amount of *work* which falls to the share of the several chambers of the heart. Thus, as already mentioned, the left ventricle is thicker than the right, and the auricles are thin in comparison with the ventricles. A similar relation between work and bulk holds good in diseased states, when, from any cause, the circulation is embarrassed and effected with unusual difficulty. A most common cause of excessive enlargement of the heart is the imperfect action of a valve, which either obstructs the free exit of blood from a cavity, or allows blood to return in consequence of imperfect closure; such an imperfection is equivalent to an addition of work, and the consequence of additional work is increased bulk of muscle. An excessive growth (*hypertrophy*) takes place gradually in response to the necessity, and the imperfection may thus be adequately compensated for a long period.

The *nervous supply* of the heart is derived from the medulla oblongata and spinal cord by two channels—the *vagus* and the *sympathetic.* Both kinds of nerve-fibres, medullated as well as non-medullated, are contained in these nerves, and numerous ganglion-cells, in some places collected into ganglia of considerable size, are situated on their course.

The hearts of cold-blooded animals, that of the frog especially, owe their physiological importance to the fact that they are easily studied. The heart of a cold-blooded animal—frog, fish, tortoise, crocodile, &c.—will continue to beat for hours after it has been cut out of the body, whereas the time during which the heart of a mammal will beat under similar circumstances is to be counted in minutes only. It is necessary to notice the points in which the hearts of cold-blooded animals differ anatomically from those of mammals, and it is advisable in the appreciation of physiological results to distinguish between such as refer only to cold-blooded animals, and others which refer only to mammals.

Thus the experiment of the 'Stannius' ligature' refers to the frog's or toad's heart; the action of the depressor nerve is experimentally known only in the case of the rabbit's or cat's heart; observations of intra-cardiac pressure have been mostly made on the dog's or horse's heart; the characters of the heart's sounds and of the pulse are studied in detail only in the case of man.

Structure of the frog's heart.—The *frog's heart* is composed of a single ventricle and two auricles. The right auricle receives the venous blood of the whole body; the left auricle receives the blood of the lungs; the venous blood of the body is carried to the sinus venosus through the three venæ cavæ, and thence into the right auricle. Both auricles open into the ventricle, which thus receives mixed blood. From the ventricle the blood is driven into the bulbus arteriosus, and thence into the system, the lungs, and the skin. The mixed blood from the ventricle loses oxygen in the system, gains oxygen in the lungs and skin. The muscular fibre of the frog's heart differs from that of the adult mammalian heart; it is of a more embryonic character, composed of long spindle-shaped cells, which are nucleated and dimly cross-striated. It closely resembles the fibre of the embryonic mammalian heart. The cavity of the ventricle is intersected in all directions by bundles of muscle, giving the mass a spongy structure; this is well seen when an inflated and dried ventricle is cut across. Nerve-fibres, medullated and non-medullated, the former derived from the vagus, the latter from the sympathetic, are abundant in the auricles and in the upper third of the ventricle. Nerve-cells, scattered and massed together as ganglia, are abundant in the same situations; they are probably in connection with medullated or vagus fibres; their principal masses are in the sinus venosus (Remak's ganglion), in the auricular system (von Bezold's ganglion), and at the base of the ventricle (Bidder's ganglion). Neither nerve-fibres nor nerve-cells have been detected in the lower two-thirds of the ventricle.

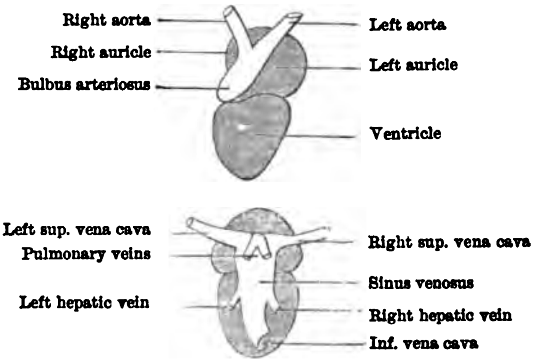


FIG. 16.—ANTERIOR AND POSTERIOR VIEWS OF FROG'S HEART. (After Cyon.)

The **heart of man** is constantly examined in hospital wards by various instruments applied to the chest-wall where the heart rests against it. The character of beat, as regards *force* and *frequency*, is judged of by mere inspection, or by the hand laid upon the chest-wall. The size of the heart is ascertained roughly by *percussion*. The sound which percussion of the chest-wall brings out is different according to the nature of what lies behind it where the heart lies behind the chest-wall the percussion-sound is far duller and less resonant than where the lung lies; an area of 'dulness' may thus be mapped out on the chest-wall, the extent of which gives some notion of the size and position of the heart.

But the most important indications are those furnished by the *sounds* of the heart, which reveal the condition of its valves if the ear is applied to the front of the chest the sounds of th heart will be plainly heard—two sounds with a rhythm resembling that of the footsteps of a man who walks lame. The *firs* *sound* is muffled and prolonged in comparison with the secon sound, which is short and sharp. Their character is imitated by the syllables *lub-dup*, but this character should be realised by applying the ear to a person's chest. To simply hear the heart's sounds it is sufficient to lay the head against a person's chest: to localise on the chest-wall the spots where the sounds are best heard, a stethoscope must be used. The sound due to closure of the mitral valve is loudest when the stethoscope is placed over the so-called apex-beat; that due to closure of the aortic valves is loudest at the second right costal cartilage. It is then easy to recognise that the first sound is simultaneous with the impulse of the heart; it occurs with the ventricular systole, and is therefore called *systolic*; thus the impulse gives an easy means of recognising the first from the second sound, if the distinction has not already been made by means of rhythm and character of sound. The second sound occurs at the end of the ventricular systole, or, in other words, at the beginning of the ventricular diastole, and it is therefore called *diastolic*. As to the cause or causes of the sounds, these have been ascertained by experiments on animals and by observations on man. The first, or systolic sound, is due to two causes combined: (*a*) the sudden closure of the auriculo-ventricular valves; (*b*) the noise of muscular contraction. The second, or diastolic, sound is caused by the sudden closure of the semilunar valves. The latter statement has been proved as follows: curved needles have been introduced through the carotid artery into the aortic orifice, and the aortic semilunar valves have been hooked back so that they could not close properly; the second sound has then lost its sharp character and become replaced by a rushing noise. On withdrawal of the needle the sharp slapping second sound has returned; therefore the second or diastolic sound is due to the sudden closure of the semilunar valves. If the valves have become permanently injured, so as to be incompetent to close the orifice when it should be closed—*i.e.* when diastole begins—the character of the second sound is permanently altered, the sharp slap is replaced by a diastolic noise, which is caused by the blood as it escapes back into the ventricle. On man such diastolic noises or murmurs are not unfrequently heard instead of a natural second sound; they indicate an incompetent state of the aortic valves, and the fact is frequently verified after death, thus affording confirmation of the statement that the second sound is due to the sudden closure of the semilunar valves.

That the first, or systolic, sound is caused by muscular contraction and by valve-closure combined, is proved by two experiments: (1) the closure of the mitral valve has been prevented by a wire ring introduced into the auriculo-ventricular orifice—the first sound was thereby much altered; or the cordæ tendinæi have been divided by a curved knife, with a similar result to the first sound. (2) A systolic sound can still be heard in the excised and empty hearts of dogs. There is here no possibility of valve-tension, and the noise made by the contracting ventricle must therefore be admitted to be a factor in the production of the first sound. (3) On man a natural first sound is not unfrequently modified or replaced by a systolic murmur; one of the causes of this, as has been verified after death, is an incompetence of the mitral valve, which does not close properly, but allows blood to escape backwards into the left auricle during the ventricular systole.

The heart's *impulse* is usually most easily felt in the fifth intercostal space, about one inch below the nipple and one and a half inch nearer the sternum. The situation of the impulse is, however, by no means invariable; it may be more marked in the fourth intercostal space, or further towards the axilla than the nipple; it alters with the movements of respiration and with the position of the body, and it is modified both in situation and extent by variation in the size of the heart. This spot, where the impulse is greatest, is often termed the 'apex-beat'—a misleading expression, for the true apex of the heart lies much deeper; a needle plunged through the spot of maximum impulse would pierce the left ventricle at the junction of the middle with the lower third. The cardiac impulse is not produced by the heart's tilting itself so as to strike the chest-wall; it is due to the sudden hardening and tension of the contracting ventricles, and the spot of impulse, or so-called 'apex-beat,' is simply the spot where the convex ventricular mass comes into contact with the chest-wall.

The impulse of the heart may further be studied by means of the *cardiograph*. This is an instrument by means of which the movement produced by the impulse is magnified and recorded as a curve on a travelling surface. A cardiograph consists of the following parts: (1) an exploring tambour, which is applied to the spot where the impulse is best felt; this tambour is joined by a tube with (2) a recording tambour which carries a lever. These tambours are like small kettledrums, with drumheads made of a very elastic membrane. Both tambours and connecting tube are full of air, and any pressure, such as that produced by the heart's impulse, exerted upon the membrane of one tambour, is transmitted through the connecting tube to the other tambour, causing bulgings of its membrane, which are magnified by the lever. The lever marks its movements against (3) a travelling surface, a usual form of which is a cylinder covered with smooth paper and blackened by a smoky flame; the point of the lever rubs lightly against this blackened surface and makes a white line, or 'tracing.' The rate at which the cylinder revolves varies according to the special requirements of observation; it is determined by means of a time-marker, or 'chronograph,' which is essentially a lever also touching the smoked paper, and moving once per second, so as to mark seconds; or 10 times per second, so as to mark tenths of a second; or 100 times per second, so as to mark hundredths of a second, &c.

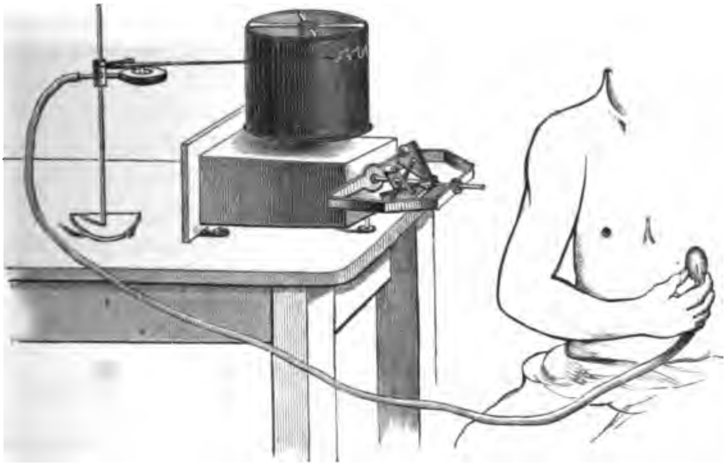


FIG. 17.—THE CARDIOGRAPH AS APPLIED TO MAN.

By means of the cardiograph we may accurately determine the time occupied by the systole of the auricles and of the ventricles, and by their diastole. The following figure gives an example of a heart-tracing thus obtained, the lower line being the time marked in tenths of a second. The auricular systole is seen as a small elevation immediately preceding the larger and longer elevation caused by the ventricular systole, the beginning and end of which is shown by the points at which the lever begins to rise and begins to fall.

If the movements of the recording lever be carefully watched while the heart's sounds are listened to, it will be apparent that the first sound is heard as the lever rises, the second sound as it falls—*i.e.* the first sound is systolic, the second sound is diastolic. Their time of occurrence has been indicated below the heart-tracing by black marks. Assuming that the heart is beating sixty times per minute, so that each cardiac event or cycle lasts one second, the systole and diastole of the auricles and ventricles will occupy the following fractions of a second:—

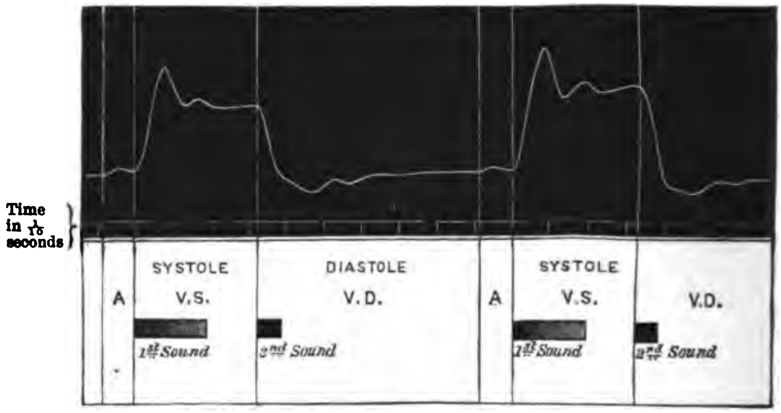


FIG. 18.—A TRACING FROM THE 'APEX-BEAT' OF MAN.

Relation of sounds to contraction indicated below the tracing.

Auricular systole	one-tenth
Auricular diastole	nine-tenths
Ventricular systole	four-tenths
Ventricular diastole	six-tenths

An increased number of beats per minute naturally implies diminished length of each diastolic pause, also—but in less degree—diminished length of each systole. With each increase of ten beats per minute, the diastole decreases by about $\frac{10}{100}$ of a second in duration, the systole by about $\frac{2}{100}$. Consequently the total systolic or working time of the heart is greater at a high than at a low pulse-frequency as compared with its total diastolic or resting time. Normally the human heart is at work for about nine hours of the twenty-four, at rest during about fifteen hours. These points are exhibited in the accompanying figure and table.

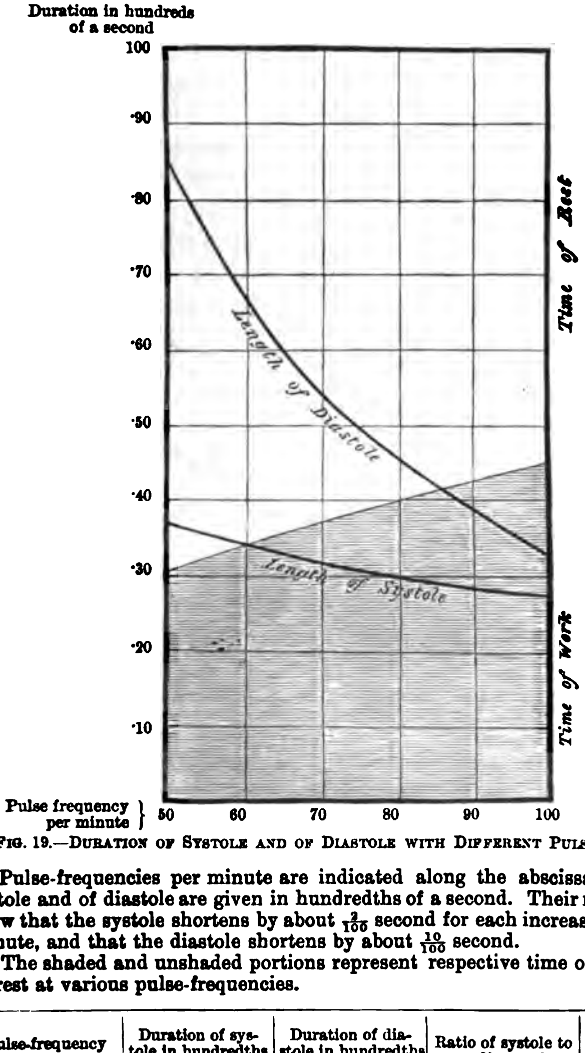


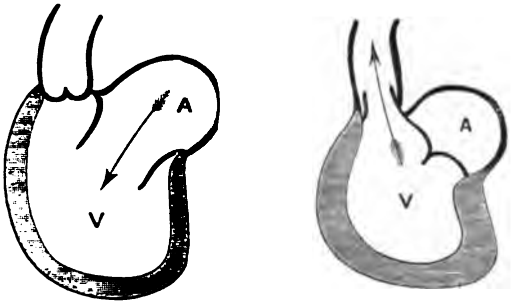
FIG. 19.—DURATION OF SYSTOLE AND OF DIASTOLE WITH DIFFERENT PULSE-FREQUENCIES.

Pulse-frequencies per minute are indicated along the abscissa. Durations of systole and of diastole are given in hundredths of a second. Their respective curves show that the systole shortens by about $\frac{2}{100}$ second for each increase of 10 beats per minute, and that the diastole shortens by about $\frac{10}{100}$ second.

The shaded and unshaded portions represent respective time of work and time of rest at various pulse-frequencies.

Pulse-frequency per minute	Duration of systole in hundredths of a second	Duration of diastole in hundredths of a second	Ratio of systole to cardiac cycle	Hours of work per diem
50	37	83	·31	7·5
60	34	66	·34	8·2
70	32	54	·37	8·9
80	30	45	·40	9·6
90	28	38	·42	10·2
100	27	33	·45	10·8

The foundation of all precise acquaintance with the mechanism of cardiac contraction—abnormal as well as normal—is summarised in the following propositions, each of which must be realised and mentally 'seen' before the details of individual cases and experiments can be understood. (1) *During* **systole** *the ventricles contract and empty themselves into the pulmonary artery and aorta; the semilunar valves of these vessels are open; the auriculo-ventricular valves are shut; the first sound is produced.* (2) *During* **diastole** *the ventricles are relaxed; the semilunar valves of the pulmonary artery are closed; the auriculo-ventricular valves are open, and the blood is flowing from auricles to ventricles; just at the end of the diastole, the auricles contract. The second sound is produced at the beginning of diastole.*



Diastole Systole

Fig. 20.—Diagram to Illustrate the State of the Cardiac Valves and of the Blood-current during the Diastole and Systole of the Ventricles.

These are the main facts, around which all others attach themselves as accessory and subordinate. Among these accessory facts are: the alterations of volume in systole and in diastole, the rotation of the contracting and relaxing ventricle, the mode of commencement of the auricular contraction, the manner in which the musculi papillares act upon the intracardiac valves and secure their perfect closure. These points may be briefly disposed of. The volume of the heart is diminished during systole, the ventricular mass in contracting becomes shorter as well as narrower, although on superficial examination the narrowing is such as to give an appearance of elongation This systolic shrinkage is accompanied by a certain amount o twisting in consequence of the spiral disposition of the muscular layers which form the ventricles; the rotation is such that the heart twists round its long axis from left to right with the systole, *i.e.* against the hands of a watch, and from right to lef with the diastole. If the auricles be closely watched when the heart is beating slowly, it will be noticed, in the left auricle especially, that the contraction starts from the venous orifices, and that it is in fact ushered in by contraction of the large veins; the auricles are anatomically as well as physiologically continuous with the large veins which open into them. The points so far considered may be verified by simple inspection of the moribund and therefore sluggishly beating heart of any recently killed mammal; the exact action of the musculi papillares under normal conditions has been until quite recently a subject of argument rather than of direct observation; from their attachment to the inner surface of the ventricle near the apex and by the cordæ tendineæ to the free edges of the curtain-like cusps of the mitral and tricuspid valves, it is obvious that they must prevent these cusps from being floated back into the auricles when the ventricles begin to contract; by their contraction they must compensate the shortening of the ventricle and thus keep the valves tight. According to Roy and Adami the papillary muscles begin to contract a little later and cease to contract a little sooner than the rest of the ventricle.

Blood-pressure.—At each stroke of the ventricles blood is driven into the arteries; its passage into the veins is impeded by the friction of the mass of blood against the walls of the capillaries, and by the narrowness of the minute arteries leading to them. The resistance thus offered is spoken of as the 'peripheral resistance.'

The *arteries* are distensible and elastic—that is to say, they can be distended by internal pressure, and they can shrink again when the internal pressure ceases. Elasticity should be carefully distinguished from distensibility or extensibility. A band of india-rubber lying loose on the table is extensible—it may be taken up and stretched, but it is not elastic until it is stretched; while held stretched between two hands it is elastic—that is to say, it is pulling the two hands together, and will shorten if let go. The arteries can be stretched by internal pressure, *i.e.* they are distensible; further, the arteries are in the living body kept stretched by the blood which is driven into them, *i.e.* they are elastic; and their elasticity is constantly exerted in pressing upon the blood. The *blood-pressure*[1] is thus the resultant of two factors—(1) the heart's force, (2) the peripheral resistance. The elasticity of the arteries may be named as a third factor, but it must be borne in mind that this recoil force is not an independent factor, but derived from the heart's force. Arterial elasticity supplies no fresh force, but simply acts as the reservoir of the heart's force; just as the distended air-bag of a piper acts as the reservoir of his expiratory efforts; its effect as regards the circulation is to convert pulsating, intermittent force into continuous force; each beat of the heart is in great part spent in keeping the arteries distended, bringing into play their elasticity which is constantly compressing the contained blood, thus keeping up a constant flow in the intervals between the beats. A part of each beat is, however, not thus spent in keeping up elasticity and pressure, but goes directly to increase pressure an onward flow; it is this portion which is manifested as the pulse and in a corresponding acceleration of the velocity of the blood current. In physical terms the beats are spent partly in main taining an arterial potential which is constantly exerting itse and becoming kinetic, partly in the direct kinetic element man fested as the pulse. The arterial blood-pressure will obviousl vary with variations of its factors—*i.e.* pressure will be greate with greater heart's force or with greater peripheral resistance and *vice versâ.*

---

[1] The term 'blood-pressure,' used without qualification, is understood to denote arterial blood-pressure.

The Manometer.—Blood-pressure is measured on animals by mean of the *manometer*, of which there are various forms; the simplest an most convenient is the mercurial manometer. A bent glass tube suitable length, half-filled with mercury, is connected with the interi of an artery, say the carotid, by means of a tube and cannula filled wi sodium carbonate solution. The blood presses through the cannu and tube towards the manometer, and causes the mercury to fall one limb and rise in the other. The difference of level at which t mercury stands in the two limbs gives the pressure of mercury equ to the pressure of blood in the case examined. If the column mercury be closely watched, or if a float carrying a pen be arranged as to record the level of the column upon a revolving cylinder, it will noticed that the height of the column is variable—irregularly variab *i.e.* rising or falling more or less without obvious cause or in con quence of muscular efforts; and regularly variable, rising and falli with each beat of the heart and with each act of respiration. T complete apparatus for taking blood-pressure records is commo termed a *kymograph.*

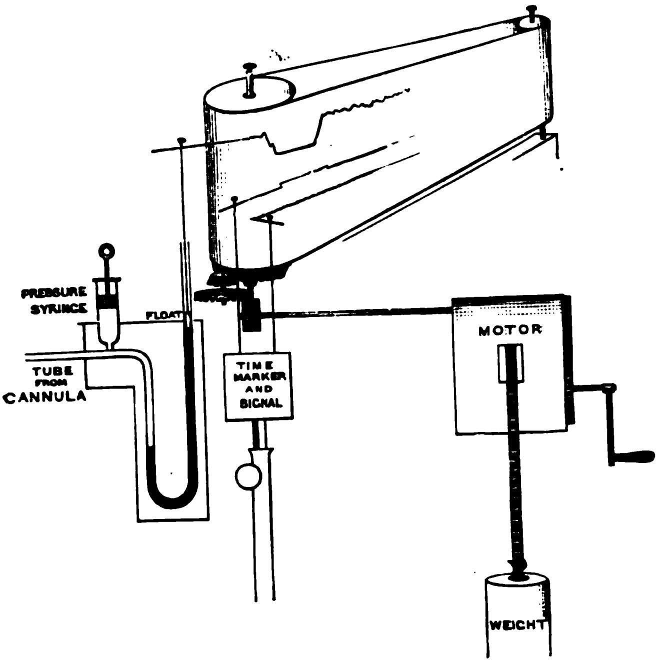


FIG. 21.—DIAGRAM SKETCH OF THE MERCURIAL KYMOGRAPH. (Hering's Model.)

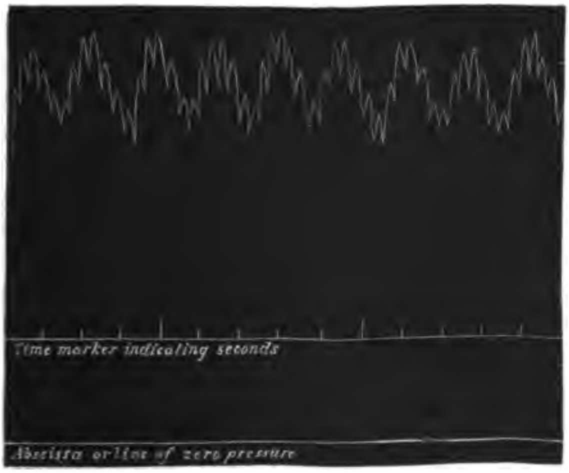


FIG. 22.—PORTION OF A BLOOD-PRESSURE TRACING FROM THE CAROTID ARTERY OF A RABBIT.

The small undulations are due to the heart-beat; the larger undulations upon which they are superposed are due to the movements of respiration. The height above the zero line is one half the blood-pressure expressed in terms of mercurial pressure.

Arterial blood-pressure cannot be studied upon man by the method above described; all direct evidence on the subject is derived from experiments on animals, such as the dog, rabbit, and horse, and from the facts thus obtained we judge of what must take place in the human arterial system. The mean blood-pressure in the carotid artery of a rabbit is equal to about 8 to 10 c.m. of mercury, of a dog or horse 12 to 15 to 20 cm.; in the human carotid artery the pressure is supposed to have about the same value, viz. about 15 to 20 cm. = 6 to 8 inches.

Attempts are indeed made to estimate arterial pressure clinically by means of the sphygmograph and other instruments such as the plethysmograph and the sphygmomanometer, but i is difficult to get exact results by any instrument, and the puls skilfully felt is the readiest means of estimating arterial pressur on man. By feeling the pulse, we may ascertain that blood-pressure is unusually high, or unusually low, or not far wrong; we sa accordingly that tension is high or low or normal, and we spea of a pulse as of high tension, or of low tension, or of norma tension.[1]

We have recognised as obvious that, *cæteris paribus*, arteria pressure should be greater with greater heart's force, less wit less heart's force, greater with greater peripheral resistance, les with less peripheral resistance. All these statements may b illustrated by experiments and observations. Violent exertio causes the heart to beat more frequently, and possibly each bea may be stronger, though this is not necessarily so, but in an case the total force exerted by the heart during a given time– say a minute—is greater than usual, and the blood-pressure temporarily increased; a sudden shock or a strong emotion, c experimental stimulation of the vagus nerve, weakens or arrest the action of the heart, and the blood-pressure is temporaril diminished. If the vaso-motor centre in the medulla is stimulate the muscular arterioles contract and narrow the outlet from tl arterial system, so that the peripheral resistance is increased blood-pressure is raised. If the vaso-motor centre is destroye or its action is depressed by shock, the muscular arterioles rela and widen the arterial outlet; blood-pressure falls.

---

[1] The word 'tension' is more commonly used in clinical medicine than t word 'pressure.' Arterial tension signifies the elastic force exerted by a distend artery; this elastic force is equal to the distending force of blood-pressure. T terms 'arterial tension,' 'arterial pressure' may therefore be substituted each the other.

Blood-flow.—All these are extreme cases, which actually do occur in the living body; but we have to recognise that the several alterations, whether of the heart or of the arteries, naturally limit and neutralise each other, so that a marked change of pressure, as above described, can only occur in consequence of an excessive alteration of one of two factors. The co-operative variations of the two factors will be better understood by taking into account how the *rapidity of the blood-flow* alters with the alterations of the heart or of the vessels. For the sake of brevity, these alterations may be cast into tabular form by the side of the alterations of blood-pressure which we are discussing. The table includes all the possible variations which may theoretically take place, the consequences in each case being denoted by the signs + or −, to signify increase or diminution.

No.	Heart	Arterioles	Blood-pressure	Blood-flow
1	Force constant	Resistance increased	+	−
2	Force constant	Resistance diminished	−	+
3	Force increased ...	Resistance constant	+	+
4	Force diminished ...	Resistance constant	−	−
5	*Force increased* ...	*Resistance diminished*	+ −	+ +
6	*Force diminished...*	*Resistance increased*	− +	− −
7	Force increased ...	Resistance increased	+ +	+ −
8	Force diminished ...	Resistance diminished	− −	− +

The first four cases need not detain us long. If—supposing the heart's force to remain constant—the arterioles contract and increase the peripheral resistance, it is obvious that pressure will be raised, and that through the constricted outlet less blood will flow (1); *vice versâ*, if the arterioles dilate, widening the outlet and diminishing the resistance, it is clear that pressure will fall, and more blood will flow through the vessels (2). If—supposing the peripheral arterioles to remain unaltered—the heart beats more strongly or less strongly, it is obvious that with more force there will be increased pressure and increased flow of blood (3), with less force there will be diminished pressure and diminished flow (4).

Turning to the next four cases, in which both factors are altered, it is evident that in (5) increased heart's force will give more pressure, while diminished peripheral resistance will give less pressure; these alterations neutralise each other, and pressure remains unaltered, or if either should exceed the other the resultant alteration, being only their difference, is not great But as regards blood-flow the result is otherwise; increase heart's force gives increased flow, diminished peripheral resistance also gives increased flow, and these two alterations unite give a resultant alteration which is comparatively great. Simila reasoning applies to the combination (6), all data and result being reversed; thus, diminished force of the heart gives les pressure and less flow, increased resistance gives greater pressur and less flow; as our resultants we have little or no alteratio of pressure, and a great diminution of the blood-flow. Thu in these two cases (5 and 6) we have a minimum alteratio of blood-pressure with a maximum alteration of blood-flo If now we consider the last two cases we shall find how di ferently the results come out. In combination (7) the increase heart's force gives increased blood-pressure, and so does th increased peripheral resistance; the resultant increase of bloo pressure is therefore considerable, while as regards the bloo flow the first factor increases, the second diminishes it, and th resultant alteration is little or nothing. In combination (similar reasoning applies; both factors diminish the bloo pressure, but the first diminishes while the second increas the blood-flow. Thus in these two cases we have a maximu alteration of blood-pressure with a minimum alteration of bloo flow.

The body, as a whole, requires, according to circumstance more or less blood; more or less blood-pressure is of its useless, and accordingly we find that the temporary variatio which naturally occur in the body are such as produce *a mi mum alteration of blood-pressure with a maximum alteration blood-flow* (viz. cases 5 and 6), whereas the converse variatio (viz. 7 and 8), giving a maximum alteration of blood-pressu with a minimum alteration of blood-flow, are abnormal and not occur in the healthy body. In diseased conditions they however occur, and persist as enduring states: in renal disea a strongly beating heart with constricted arterioles and con quently high blood-pressure, form a very usual combination ; great prostration from any cause, a weak heart with rela arterioles, and consequently low blood-pressure, is the invaria rule. And it may be incidentally noticed how in these cases t two factors add themselves as regards blood-pressure but opp and compensate each other as regards blood-flow, so that t body is not starved of blood in the same proportion as the circulation becomes weaker (case 8); nor over-supplied with blood in proportion to a heightened blood-pressure (case 7). Referring to the table we see that in these combinations a minimum alteration of blood-flow accompanies a maximum alteration of blood-pressure. Thus analysed we can recognise the economy of the relationship between the state of the heart and of the vessels, and between blood-pressure and blood-supply. The essential event is blood-supply, to which blood-pressure is subservient. Normal fluctuations of tissue-activity elicit corresponding fluctuations of blood-supply with minimum alterations of pressure. Abnormal alterations of blood-pressure do not, until they are excessive, interfere with a normal and necessary rate of blood-supply.

It should, however, be added that the immediate effects of increased or diminished blood-pressure are always an increase or a diminution of blood-flow, although in the first case the vessels are constricted and in the second case dilated. This is a result which we could not foresee on *a priori* grounds, but which has been established by experiment; destruction of the spinal bulb relaxes the arterioles, lowers blood-pressure, and reduces blood-flow; excitation of the bulb constricts the arterioles, raises blood-pressure, and accelerates blood-flow. Both these facts have been ascertained by direct measurement of the aortic blood-current.

Local variations.—The general requirements of the whole body vary, and are met, as above described, by variations of the general blood-pressure and blood-flow, variations of flow being more important than variations of pressure. We have further to consider *local variations* in response to the particular requirements of its several parts or organs. Two different parts or organs may at the same time require very different amounts of blood, the same part or organ requires at different times very different amounts of blood. Such local variations of requirement are met by local variations of the peripheral resistance, the arterioles of the part or organ contracting when less blood is required, relaxing when more blood is required. A gland during secretion, a muscle during contraction, the digestive viscera during digestion, the brain during mental exertion, require and receive more blood than the same parts while at rest; their arterioles dilate, the blood-flow through them is increased, more food is received during more work. Such local changes may o may not affect the general circulation, according to their magnitude or rate of occurrence. If the changes occur in a sufficientl large district—as, for instance, in the area governed by th splanchnic nerves, *i.e.* the intestinal vessels—the effects will b as follows: a contraction occurs of the splanchnic area, th blood-pressure of that area rises, the general blood-pressur shares in that rise of pressure, less blood passes through th splanchnic area, more blood passes through the remainder o the system; or a dilatation occurs of the splanchnic area, blood pressure falls in that area and elsewhere throughout the body– more blood passes through the splanchnic area, less blood passe through the system. This last series of effects is indeed precisely what takes place after every copious meal; blood is the diverted to the intestinal vessels, there is less blood than usua in the remainder of the system; a feeling of chilliness and disinclination to exertion, mental or physical, are the token that much blood is engaged in visceral action and cannot b spared to other parts; or, if the disinclination be overcome, if b forced exertion blood be called to the brain or to the limbs, the the visceral blood-flow is made insufficient, and digestion i disturbed.

Addition and removal of blood.—It might appear at fir sight that the blood-pressure should be relatively high when th system contains more blood than usual, relatively low when contains less blood than usual. Yet in the living body this do not necessarily hold good; a large quantity of fluid may b injected into the arterial system without causing any increa of blood-pressure, and an animal may be copiously bled witho lowering the blood-pressure. It is not until the excess deficiency are pushed to extremes—*i.e.* the total amount near doubled or halved—that any effect is produced, and then dea usually follows. These facts are of importance, for they sho that the arterial system, by contraction or by relaxation of i muscle, can accommodate itself to very different quantities blood without alteration of pressure, and that we should n attempt to reduce a high blood-pressure by removing blood, or raise a low blood-pressure by injecting blood or other fluid. T total quantity of fluid present in the vascular system is, mo over, kept very uniform by osmotic currents which trans water from lymph to blood after a loss of blood, or from blo to lymph after an injection of fluid into the vascular system. In as short a period as half an hour after copious hæmorrhage, the dilution of the remaining blood is recognisable by a marked diminution of specific gravity; and the opposite effect—viz. recovery from dilution after an injection of fluid—is seen in the no less rapid restoration of a lowered, to the normal specific gravity.

The blood-pressure *in the capillaries* is approximately measured by determining the amount of compression which is required to blanch a portion of flushed skin, *i.e.* to empty its capillaries ; 2 centimeters of mercury is an average value.

The blood-pressure beyond the capillaries, *i.e. in the veins*, is exceedingly small and variable; in the jugular vein it is about ½-centimeter above and below zero in expiration and in inspiration respectively. There is danger of the entrance of air into a vein in operations at the root of the neck, owing to this negative pressure during inspiration.

The blood-pressure *in the heart* itself, differs in the different chambers and oscillates with systole and diastole ; these oscillations succeed each other so rapidly that the mean pressure as recorded by a mercurial manometer is considerably lower than the real maximum within the ventricle during systole. By means of a manometer guarded by a valve arranged so as to prevent the column of mercury from falling after having been raised by systolic pressure, Goltz and Gaule determined the maximum intraventricular pressure, *i.e.* that obtaining during ventricular systole; on reversing the valve, so that the column could fall but could not rise, they determined the minimum intraventricular pressure, *i.e.* that obtaining during ventricular diastole, and found that this minimum pressure was negative—in other words, that the ventricles have a suction action in the diastole. The following pressures were observed :—

	Maximum in systole	Minimum in diastole
Left ventricle . . .	+ 15 cm. Hg.	– 5 cm. Hg.
Right ventricle . .	+ 6 cm. Hg.	– 1·5 cm. Hg.

By means of improved manometers, in which inertia is reduced to a minimum by the substitution of a spring for the heavy mercury, records of intraventricular pressure have been obtained which may be considered as accurate representations of its variations in the several phases of the beat. Fig. 23 is an example of such a record; it shows the magnitude and duration of positive systolic and of negative diastolic pressure. In the auricles, except during their systole, the pressure does not exceed that in the large veins; hence even a small pressure within the pericardium will cause the auricles to collapse. The maximum systolic pressure in the left and right auricles amounts to about 5 and 2 centimeters of mercury respectively. Obstruction to the arterial circulation, as by compression of the aorta or by vaso-motor spasm, raises the pressure in the left auricle to such an extent that it ceases to contract.

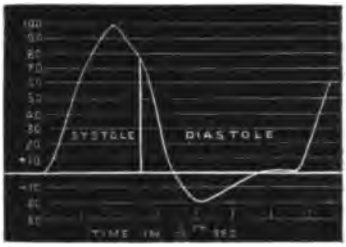


FIG. 23.—INTRAVENTRICULAR PRESSURE OF DOG'S HEART.

Positive during systole, negative during the first part of the diastole. The numbers and horizontal lines indicate pressure in mm. Hg.

Influence of varying arterial pressure upon venous and upon pulmonary pressure.—As might be expected, the general venous pressure has been found to rise with a fall of arterial pressure, and to fall with a rise. The mechanism of the relation is as follows: (1) if the fall of arterial pressure is due to reduced action of the heart (*e.g.* by vagus excitation), blood accumulates in the great veins and pressure rises; (2) if the fall is due to dilatation of systemic arterioles, blood passes with greater facility into the veins, and pressure rises; (3) if arterial pressure is raised by increased action of the heart (*e.g.* after section of vagi), blood must be taken from the great veins with increased rapidity, and pressure will fall; (4) if a raised pressure is caused by constriction of arterioles, less blood passes into the veins, and pressure falls.

There are, however, exceptions to this rule; the effects on venous pressure of a dilated or contracted outlet of the arterial system may be masked by the effects of the increased or diminished capacity of the arteries caused by their diminished or increased tonus; if the medulla oblongata be destroyed or the splanchnic nerves be cut, venous as well as arterial pressure will fall, because blood accumulates in the relaxed abdominal vessels; if the medulla or splanchnic nerves be stimulated or the abdomen compressed, venous and arterial pressures will be raised, because blood is squeezed from the abdominal vessels into the rest of the vascular system. It is also obvious that a fall or rise of pressure, caused by hæmorrhage or by injection, will, if effectual at all, lower or raise venous with arterial pressure. Apart from these exceptions, the general rule holds good, that venous pressure falls with a rise and rises with a fall of arterial pressure. We shall find this relation illustrated in the alterations of pressure which accompany the movements of respiration; it is also well shown by 'Traube-Hering' curves, the pressure falling and rising in the veins as it rises and falls in the arteries (pp. 141, 145).

Alterations of pressure in the systemic vessels will influence the pressure in the pulmonary vessels in the same sense as in the systemic veins, and in a similar manner as a consequence of greater or smaller onward flow; pressure in the pulmonary circuit will thus rise with a fall, and fall with a rise of aortic pressure. These effects are, however, very much reduced by the great distensibility of the pulmonary vessels, which can accommodate a large addition of fluid without sensible rise of pressure, and which will permit the passage of an undiminished volume of blood, when the vascular channels have been experimentally reduced to less than one-half their sectional area (Lichtheim). It is to be observed, moreover, that a rise or a fall in pulmonary blood-pressure, due to free or limited supply of blood from the systemic veins, due in turn to free or limited arterial outlet, may be counter-balanced or even reversed, by the retrograde effect of diminished or increased systemic obstruction; greater aortic pressure may in this way cause a rise in place of a fall of pulmonary blood-pressure. In sum, the blood-pressure, and the resistance in the pulmonary circuit are low and constant, and very little influenced by variations of aortic pressure.

The reverse relationship, *i.e.* the effect of varying pulmonary pressure upon aortic pressure, is of more importance. We shall find in studying the effects of respiration upon circulation, that alterations of pressure in the air-passages, by pressing upon or by expanding the pulmonary vessels, can drive on the blood, or obstruct its passage, and so lead to a rise or to a fall of aortic blood-pressure. This is particularly the case in laboured respiration, and is illustrated in an extreme degree by Muller's and by Valsalva's experiments (p. 143).

Further physical considerations.—A drop of water starting from the level A, will by the time it has fallen through the space H to the level B, have a velocity $=\sqrt{2\,G\,H}$. (G represents the acceleration per second under the influence of gravity, and is equal to 32 feet or 9·8 meters.)

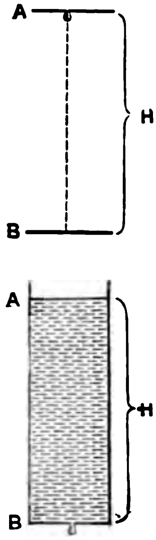


FIG. 24.

A drop of water starting from an orifice in B of a vessel of water filled up to A will have at B the same velocity as if it had fallen freely from A, viz. $\sqrt{2\,G\,H}$. This is Torricelli's theorem.

Water escaping along a horizontal tube of uniform calibre from a reservoir in which a constant level is maintained, would travel with the uniform velocity of $\sqrt{2\,G\,H}$ at all parts of the tube, *if there were no resistance.* But there is resistance at the inlet, along the tube, and at the outlet, in consequence of which the flow is retarded and a lateral pressure is maintained within the tube. This lateral or resistance pressure is indicated by the height to which water will rise in the vertical tubes 1, 2, 3. Omitting, for the sake of simplicity, the resistances at inlet and outlet, it will be seen that the levels in the three vertical tubes will diminish uniformly; the level in 1 indicating the lateral pressure produced by resistance in the horizontal tube from 1 to outlet; the level in 2 that produced by resistance from 2 to outlet, &c. The total height or pressure, H, is divisible into two parts, h and h', h being the pressure which is due to resistance, h' being the pressure which produces flow, or the 'velocity pressure.'

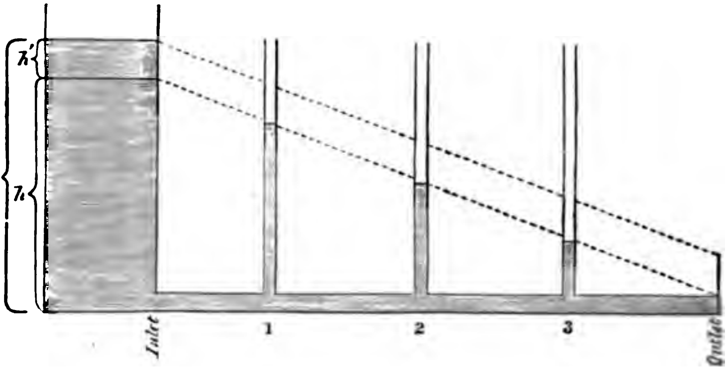


FIG. 25.

The mean velocity, which is uniform, is ascertained by experiment; its value per second is equal to

$$\frac{\textit{Volume of outflow}}{\textit{Time in seconds} \times \textit{sectional area}} \quad \text{or} \quad \frac{Q}{t\,\pi\,r^2}.$$

From the ascertained velocity the velocity-pressure, h', is calculated by

$$V = \sqrt{2 G h'} \quad \text{or} \quad h' = \frac{V^2}{2G}.$$

Water ejected from a syringe with an internal pressure measured by the height of the column, H, would have the velocity $\sqrt{2GH}$ *in the absence of any resistance.* But the velocity as observed would be much less, owing to resistance at the inlet, *i*, along the tube, *t*, and at the outlet, *o*. The total pressure, H, is divisible into two parts, *h* and *h'*, *h* being expended upon resistance, *h'* upon onward movement or velocity. The actual value of the velocity is only $\sqrt{2 G h'}$.

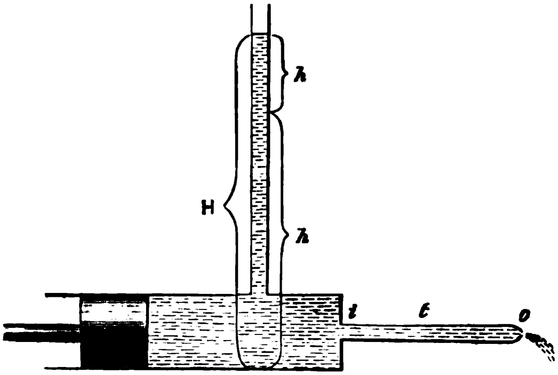


FIG. 26.

Along a tube of varying calibre the mean velocity will be greater in narrow than in wide portions, viz. inversely proportional to the sectional area πr^2.

At any given section of a tube, the velocity will be greater in the axis than at the circumference of the current. The *mean* velocity is an average value less than the greatest velocity in the axis, greater than the smallest velocity at the circumference.

Transferring these considerations to the heart and blood-vessels, we recognise that the total cardiac pressure expends itself, 1st, in overcoming resistance (h), 2ndly, in driving on the blood (h'). The value of h is given by a manometer placed in connection with a large artery;[1] the value of h' is calculated from the observed velocity by the formula $h' = \frac{V^2}{2\,G}$; *e.g.* the velocity in a carotid artery having been observed to be 30 cm. per second, the value of the velocity-pressure h' will be $\frac{30 \times 30}{1960}$ or ·46 cm. H_2O or ·035 cm. Hg; taking the lateral blood-pressure at 14 cm. Hg, h' is seen to be only $\frac{1}{400}$ of h. Thus of the tota cardiac pressure, H, on large mammals and therefore presumably or man, by far the larger part constitutes the portion h by which resistanc is overcome, the portion h', by which blood is driven onwards being onl $\frac{1}{400}$ part of the lateral pressure h, or of the total pressure H. The actua velocity in a large artery under average conditions of pressure an resistance is only $\frac{1}{20}$ of the value which it would have with the sam pressure, but with zero resistance; the theoretical value of the velocit in the absence of resistance is $\sqrt{2\,G\,H}$, the actual value in a larg vessel is about $\frac{1}{20}\sqrt{2\,G\,H}$. The recognition of this fact is of practica importance: the velocity in an unopened carotid is about 30 cm. pe second, whereas in a freely divided artery, with the resistance reduce almost to zero, it will (omitting any correction for reduced pressure approximate towards the value 600 cm. per second.

---

[1] It appears at first sight as if the total pressure H is measured when a simple cannula is placed in the cardiac end of a divided artery, and the resistance-pressure *h* only, when a T-shaped cannula is placed in the course of an artery. In the first case there is no current in the vessel; in the second, blood is flowing as usual; but practically there is no distinction between the two methods, which both give the resistance-pressure *h*. With the simple cannula in the cardiac end of an artery, the whole artery is equivalent to a lateral tube springing from a vessel in which

It is not possible to obtain the normal current velocity in an arter by measurement of the quantity of blood escaping from its cut end i a given time. From such measurement it would indeed be possible t estimate velocity in the divided artery, but this would give no inform tion as to the normal velocity in the undivided vessel. The veloci of current in a divided carotid, which we have seen is theoretical twenty times as great as in the undivided vessel, is actually five ten times as great, owing to the fact that resistance is not reduced zero, nor pressure fully maintained. From this consideration we m realise with what rapidity the blood will escape when a large artery divided. Taking the sectional area of the carotid artery as ·8 squa centimeter, the amount of blood passing through the normal ves will be 30 × ·8 or 24 c.c. per second, but hæmorrhage from the divid vessel would be at the rate of 120 to 240 c.c. per second. The ent amount of blood in a man's body is about 5,000 c.c.; the loss of h that amount is fatal; the time of grace after accidental division of a la artery, during which life can be saved, is therefore to be counted seconds, and even from a small artery blood escapes with alarmi rapidity.

In the veins the conditions are different; the resistance is sm the lateral or resistance pressure is low; the velocity of outflow fro

---

blood is flowing. Besides, as stated in the text, the difference between a t pressure H, and a lateral pressure h in a normal artery, is so small as to negligible.

divided vein scarcely, if at all, exceeds the velocity of flow within an undivided vein. On the other hand, comparing the velocities in the undivided vein, and in the undivided artery, no great difference is found —*e.g.* in the carotid the velocity is about 30 cm., in the jugular it is about 20 cm. per sec.

The relation between velocity and pressure differs in large tubes and in small tubes (*i.e.* less than 1 mm. diameter). In large tubes the velocity of stream varies as the square root of the pressure; *i.e.* with pressures of 1, 4, 9, 16, the corresponding velocity will be 1, 2, 3, 4. In small tubes the velocity of stream varies as the pressure; *i.e.* with pressures of 1, 2, 3, 4, the corresponding velocities will be 1, 2, 3, 4,; moreover in small tubes variations of diameter sensibly influence the velocity, while in large tubes such variations have no effect; with constant pressure the velocity in small tubes varies directly as the radius squared; *e.g.* if blood runs at the rate of 1 mm. per sec. through a capillary with a radius of 5 μ, it will run at the rates 4, 9, 16, 25, 36 mm. per sec. in vessels with radii of 10, 15, 20, 25, 30, μ; thus the pressure in a network of minute vessels being uniform, the blood will run much faster through the largest than through the smallest channels.

The average velocity of the blood-flow through the capillaries is ½ to 1 mm. per second; this very low velocity, as compared with the velocities in the carotid and jugular vessels, is owing to the much larger sectional area of the total capillary bed as compared with the sectional area of arteries or veins near to the heart, and to the much greater lateral friction which the blood encounters in the minute channels.

In the living body the relation between pressure and velocity is variable and complex, and chiefly dependent upon variations of peripheral resistance; as we have already seen, greater resistance produces greater pressure with smaller velocity, smaller resistance produces smaller pressure with greater velocity. Moreover, the outflow from the large arteries, and therefore the velocity within them, depend upon the minute arteries and capillaries, which govern pressure and flow in the larger pipes; *cæteris paribus*, therefore, the velocity of arterial blood-flow must vary as pressure, and not as square root of pressure; thus an organ without variation in the diameter of its arterioles will be supplied by double or by half as much blood if the general blood-pressure rises to double, or falls to half its normal value; if, with the rise of pressure, the arterioles of the organ itself should dilate, the organ will be still more copiously supplied; or if, with fall of general pressure, the arterioles contract, supply will be still further reduced. Velocity of arterial or venous blood-flow may be ascertained by direct observation; quantity of blood flowing through an artery may be calculated from the measured velocity and sectional area.[1] Thus, given the velocity of current in a carotid artery as 30 cm., the diameter of the vessel as 1 cm., we shall have the quantity of blood flowing through it equal to 30 × 3·14 × ¼ or 23·55 c.c. per second. Or again, taking the collective sectional area of the feeding arteries of the brain at 30 square millimeters, we should find, as the amount of blood received by the brain per second, a quantity of about 9 c.c.

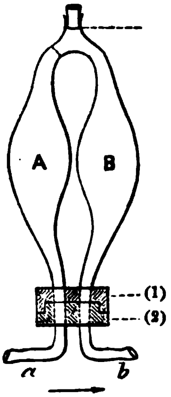


FIG. 27.—LUDWIG'S STROMUHR.

Two bulbs A and B fixed to the upper metal disc (1); two cannulæ *a b* fixed to the lower metal disc (2); the upper disc moveable round the lower, so that the connection between the bulbs A B and the cannulæ *a b* can be reversed, or interrupted. Cannula *a* fixed in central end of carotid, cannula *b* in peripheral end: bulb A filled with oil, bulb B with defibrinated blood. Blood from the central end of artery enters A, drives oil over to B, from which the defibrinated blood is driven into the peripheral end of artery. A being full of fresh blood, B is full of oil: the position of the bulbs is suddenly reversed by a half-revolution of the upper disc. B (full of oil) is now connected with *a*; A (full of blood) is connected with *b*. The manœuvre is repeated several times.

Given the capacity of a bulb, the number of times it has been filled and emptied, and the sectional area of the artery, the *velocity* of the blood-current is calculated.

Or proceeding otherwise, the quantity of blood passing through an artery may be ascertained by direct observation; velocity is then calcu-

---

[1] To calculate the sectional area of a vessel, measure its diameter, square half this number, and multiply by 3·14—*i.e.* sectional area = radius^2 × π.

The sectional area of a distended vessel is greater than that of an empty vessel —*e.g.* the carotid artery at a distension pressure of 20 cm. of Hg has about twice the sectional area of the same vessel at zero pressure.

	At 0	At 20 cm.
Capacity	1·9 c.c.	5·46 c.c.
Length	50 mm.	70 mm.
Diameter	7 mm.	10 „
Sectional area	38 sq. mm.	78 sq. mm.

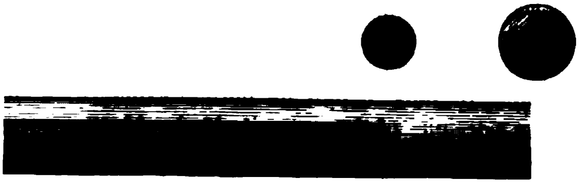


FIG. 28.

Human carotid artery at zero pressure (dark shading), and distended by a pressure of 20 cm. Hg (light shading).

lated from the measured quantity and sectional area of the artery employed.

Such measurements have been made by Volkmann, Vierordt, Chauveau, Ludwig, and by many others, and the chief instruments used have been the *hæmotachometer* of Vierordt, the *hæmodromometers* of Volkmann and of Chauveau, the *stromuhr* of Ludwig. The principle upon which the determination depends in the instruments of Vierordt and of Chauveau is the greater or smaller deflection of a pendulum by the more or less rapid stream of blood. By Ludwig's stromuhr the actual amount of blood passing through an artery in a given time is measured. The rate of current in the vessel is calculated from this amount, taking into account the sectional area of the artery employed, *e.g.* a stromuhr placed on a carotid artery of a small dog showed a flow of 90 c.c. per minute, *i.e.* 1·5 c.c. per second. The sectional area of the vessel was 5 square mm., *i.e.* $\frac{1}{20}$ square cm. The rapidity of the current is, then, 1·5 divided by $\frac{1}{20}$, *i.e.* 30 cm. per second.

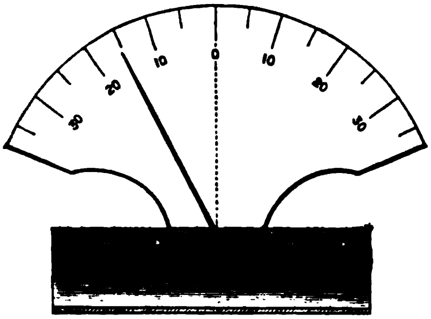


FIG. 29.—CHAUVEAU'S HÆMODROMOMETER.

The stromuhr is best adapted for giving information concerning the total amount of blood traversing an artery. The dromometer or dromograph shows the rapid variations of blood-flow which accompany rapid variations of pressure. A better instrument in use for this purpose is based upon the difference of pressure produced in 'Pitot's tubes.' In fig. 30, 1, 2, and 3 are Pitot's tubes in a long pipe leading from the bottom of the reservoir R. If there is no resistance at the outlet the water will stand at the levels *a*, *a*, *a* in the three tubes; if the outlet is closed the water will stand at the levels *c*, *c*, *c*; if the outlet is partially open the water will stand at some such level as *b*, *b*, *b*. With a free outlet and maximum outflow, the difference between any two levels *a*, *a* is at a maximum; with a closed outlet and no outflow there is no difference between any two levels *c*, *c*. Between these two extremes it is obvious that the difference of level between any two tubes *b*, *b* will be greater or smaller as the outflow is greater or smaller, in other words the difference indicates rate of flow. It is, moreover, obvious that any constriction, say at x, will increase the differences of water level in the two tubes 1 and 2.

Variations of blood-flow can be determined upon this principle.

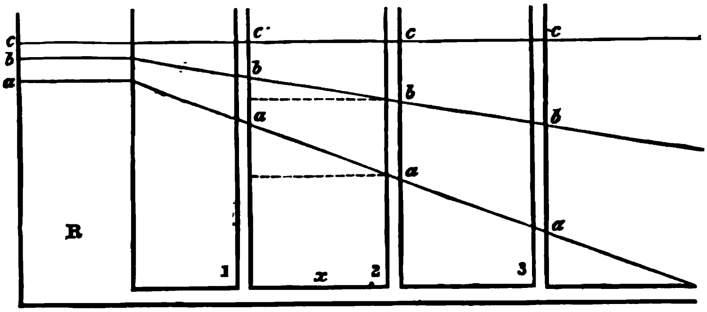


Fig. 30.

A cannula (fig. 31), with two lateral branches, A, B, and an intermediate constriction, x, is fixed in the artery. Tubes from A and B lead to two manometers. The level in the manometer connected with A will be higher than in that connected with B, and the difference will be greater or smaller according as the velocity is greater or smaller. If the two manometers be fixed in front of each other before a slit in a screen, the upper surfaces of the two columns can be photographed on a travelling sensitive surface, set up in a dark chamber behind the screen, and the varying difference between the two manometer levels thus recorded.

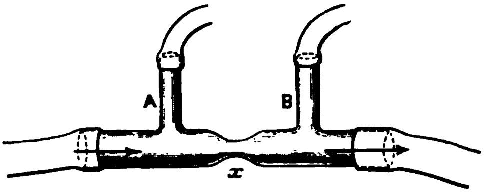


Fig. 31.

The time of circulation, *i.e.* the time which is occupied by one complete circuit of the whole mass of the blood, or—what practically amounts to the same thing—the time taken by any drop of blood to accomplish one complete circuit, is ascertained by injecting an easily recognisable salt (ferrocyanide of potassium or preferably ferrocyanide of sodium) into the jugular vein of one side, and measuring the time which elapses before the salt is detected in the blood flowing out from the other jugular. During the interval between injection and detection of the salt, the latter has been conveyed with the blood through the right heart, pulmonary vessels, left heart and systemic vessels, *i.e.* through one entire circuit. Hering, by whom this method was first employed, found that the time is greater in large than in small animals, but that it corresponds very constantly with a definite number of heart-beats, viz. 28. Thus, for instance, in a horse with a pulse-frequency of 42 per minute, the time was 40 seconds; in a rabbit, with a pulse-frequency of 168 per minute, the time was only 10 seconds; *i.e.* in each case the circuit was accomplished with 28 heart-beats. Transferring this datum to the human subject with a pulse-frequency of 70 per minute, we obtain 24 seconds as the time of circulation. The estimate so formed is obviously only an approximate one; several accessory factors influencing the actual results are necessarily neglected; thus the possible diffusion of the salt is not taken into consideration, nor the fact that different portions of the blood must traverse the circuit comparatively quickly by way of the head, and comparatively slowly by way of the portal vessels.

The capacity of the heart's chambers.—Measurements of the capacity of the auricles and of the ventricles taken after death are valueless or misleading, because the amount of fluid which these cavities will contain varies with their more or less contracted state, and is no measure of their working or functional capacity during life. We can however indirectly form such an estimate from various other data and considerations.

(1) Admitting as data, a total mass of blood in the body=5,000 c.c., and 28 heart-beats required to send this mass once round the circuit, we obtain 178 c.c. as the amount which must be expelled by each ventricle at each contraction. This amount corresponds with the estimate generally quoted on the authority of Volkmann to the effect that each ventricle discharges at each beat an amount of blood equal to $\frac{1}{400}$ the body-weight, *i.e.* in a man of 70 kilos each ventricle discharges 175 grammes of blood. But the estimate is probably too high. The number 28 expresses the quickest time in which ferrocyanide passes round the vascular system, and it is probable that the salt has made its appearance before the entire mass of blood has passed round, for diffusion has not been taken into account, nor the amount of blood which has lagged behind in the abdominal vessels. Howell and Donaldson estimate the ventricular discharge at $\frac{1}{700}$ the body-weight, a fraction which is probably nearer the truth than $\frac{1}{400}$, *i.e.* in a man of 70 kilos each ventricle would expel at each beat 100 grammes, or nearly 4 ounces.

(2) A supplementary estimate, although not in itself of much weight, may be formed from other data. Assuming (1) the rate of the blood-current in the aorta=30 cm. per second, (2) the sectional area of the aorta=5 sq. cm., we must have flowing through the aorta 150 c.c. per second, or 9,000 c.c. per minute; *i.e.* with the heart beating at 72 per minute, the left ventricle must discharge at each beat 125 c.c., or rather over 4 ounces.

(3) An entirely different series of data can be utilised to form an estimate of the ventricular capacity. We shall find in the study of respiration that the average amount of oxygen absorbed is 375 c.c. per minute, and we may assume that arterialised blood returning from the lungs contains 5 c.c. per 100 more oxygen than venous blood. Under these conditions the amount of blood by which the absorbed oxygen is carried off will be 7,500 c.c.; *i.e.* with the heart beating at 72 per minute, the right ventricle will discharge 104 c.c. of blood at each beat. We shall probably be not far from a true estimate, by taking the average value of the discharge from each ventricle at each systole to be about 4 ounces, or rather over 100 c.c.

It is obvious that the working capacities of the two ventricles must be equal, for if at each contraction one ventricle discharged more blood than the other, the systemic circuit would become emptied and the pulmonary circuit filled, or *vice versâ*. It is also obvious that the working capacity of an auricle must be somewhat less than that of a ventricle, for the ventricle when filled contains blood which has overflowed from the auricle as well as the blood which is discharged into it by the auricular contraction.

Work of the heart.—The 'work done' by a contracting muscle is expressed by the *height* to which a weight is raised. In the case of the heart, the weight raised is the amount of blood contained in the ventricles, the height to which that weight would be raised is the height of intraventricular blood-pressure during systole. From these data it is easy to calculate the 'work' done at each systole, and knowing the pulse-frequency the average per hour or per day is also known. Admitting for the left ventricle an average discharge of 120 grammes, and a systolic pressure of 2 meters of blood (about 15 centimeters Hg), the work done at each contraction will amount to 250 grammeters;[1] to this amount we may add 80 grammeters as the work done by the right ventricle and by the two auricles, making up a total of 330 grammeters or ⅓ kilogrammeter as the work done by the heart at each beat With a pulse-frequency of 72 per minute this would amount to 1,440 KgM. per hour, or more than 30,000 KgM. per diem. This is a good day's work, being one-fourth of the amount yielded by a labourer working under supervision for eight hours. The whole of this energy is expended in the body, partly in overcoming resistance in the vascular system, and partly transformed into and discharged as heat; in this form the contractions of the heart yield about 75 calories to the tota daily discharge of 2,400 calories.

Distensibility of different vessels.—The most distensible vessels are the pulmonary artery and its branches; the least distensible vessels are the systemic veins; the systemic arteries occupy an intermediate position in this respect, being less distensible than the pulmonary artery, more distensible than a systemic vein. The distensibility of an artery differs moreover from that of a systemic vein in this respect: a series of pressures of 1, 2, 3, 4, . . . &c., cm. Hg will cause on the artery a series of expansions at first increasing and then diminishing, on the vein a series of expansions which decrease from the first. According to Roy (who has shown that weighted strips of arteries behave in a similar manner) the turning-point, indicating the maximum of distensibility, coincides with the normal arterial pressure.

---

[1] If the pressure were of water, this number would be 240; the S. G. of blood (1·05) is taken into reckoning.

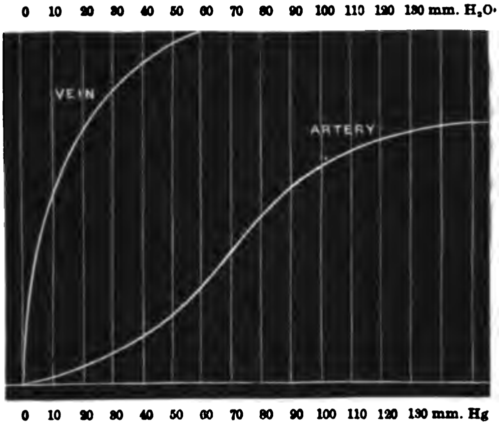


Fig. 32.

Capacity curve of a vein distended by regularly increasing pressures from 1 to 60 mm. H_2O; the same of an artery distended by pressures from 1 to 150 mm. Hg. (After Roy.)

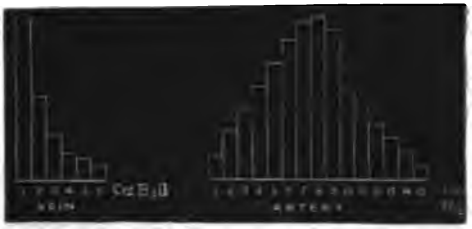


Fig. 33.

Increments of arterial and of venous capacity caused by equal increments of pressure. (After Roy.)

The plethysmograph; the oncometer.[1] A method which has been much used of late years to study the circulation is that which is based upon measurement of the varying volume of parts or organs, by means of the *plethysmograph* (Mosso) and the *oncometer* (Roy). The plethysmograph is applicable to an arm or leg, or to a single finger; the part is enclosed in a rigid vessel full of water and communicating by a tube with an open vessel which is graduated or which contains a float. As the limb swells, water is driven into the graduated vessel or raises the float; as the limb shrinks, water is drawn from the graduated vessel, or lets the float fall; when used as a recording instrument the float is connected with a light lever which traces its movements on a smoked cylinder. The oncometer is applicable to the spleen and kidney; the

---

[1] πληθύω, to swell; ὄγκος, bulk.

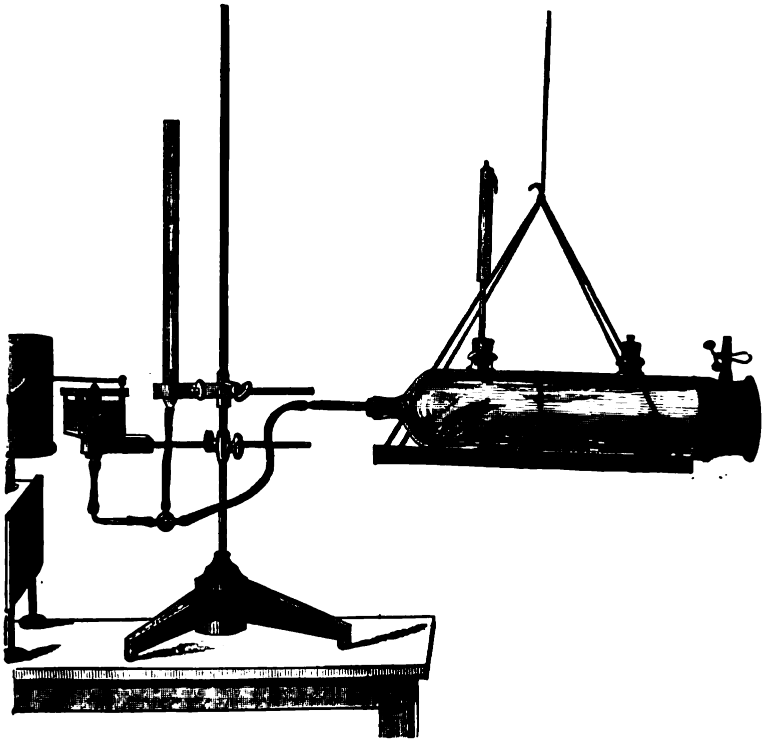


FIG. 34.—MOSSO'S PLETHYSMOGRAPH.

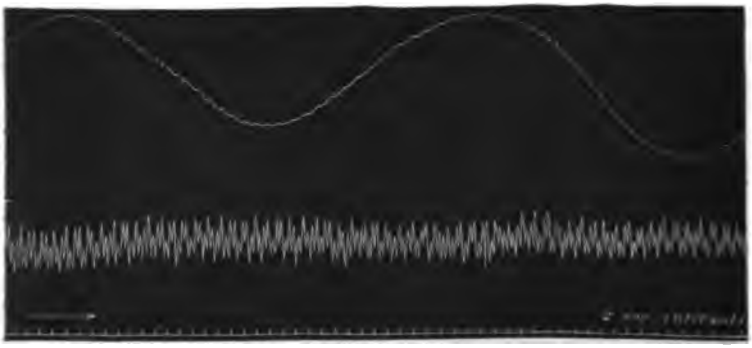


FIG. 35.

Simultaneous tracing of spleen volume (upper line) and of arterial pressure (lower line); rhythmical contractions of the spleen without sensible variations of arterial pressure. (Roy.)

complete instrument is composed of two parts—the oncometer, which encloses the organ, and the oncograph, which records the movements

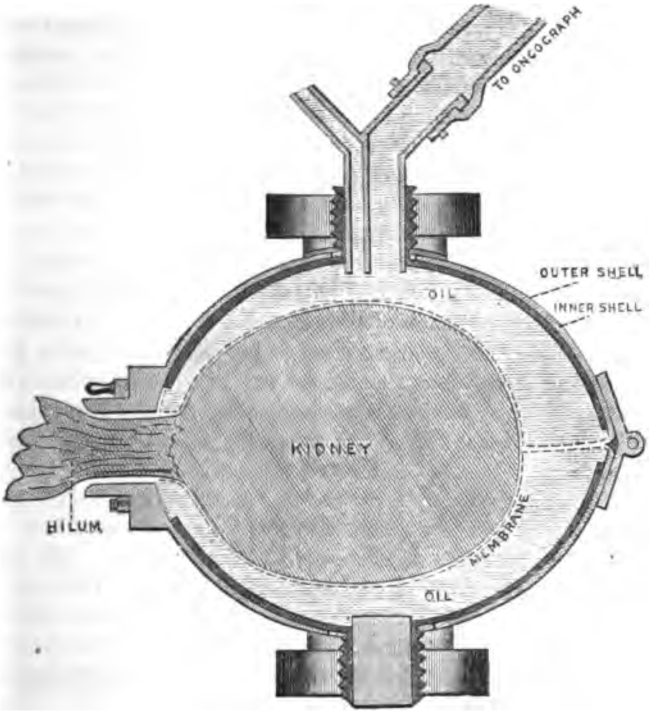


FIG. 36.—ROY'S ONCOMETER.

of a piston; the two parts communicate by a tube, and the whole apparatus is filled with oil.

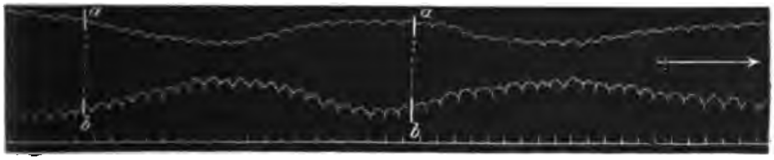


FIG. 37.

Simultaneous tracing of kidney volume (upper line) and of arterial pressure (lower line); the large undulations are Traube-Hering effects; with the rise and fall of arterial pressure the kidney volume falls and rises. (Roy.)

Variations of volume do not by themselves yield simple and unequivocal data, but require to be supplemented by readings of arterial and of venous blood-pressure. The variations in volume of a part or organ may be either active or passive; the volume of an arm, for instance, may be increased by dilatation of its arterioles or by obstruction of its veins; it may be diminished by constriction of its minute arteries, or by obstruction of its main artery. Generally speaking the volume of a part or organ increases and diminishes with its functional activity, greater activity being accompanied by dilatation of the vessels, less activity or rest by constriction of the vessels. These are active variations effected by the vasomotor nerves of the part itself. But passive variations may also be produced, in consequence of variations of the general blood-pressure brought about by vasomotor nerves in other parts of the body. The kidney for instance may shrink or swell with a rise or with a fall of blood-pressure. If it shrinks with a rise or swells with a fall, these variations are local active changes due to constriction or to dilatation. If it shrinks with a fall and swells with a rise (as occurs after section of the renal nerves), these variations are local passive changes of an organ more or less distended by the general blood-pressure. And when the nerves are intact the volume of the organ may either vary in the same sense as the general pressure, or in an opposite sense, according as the general pressure-changes overbear the local actions, or as the local actions exceed the general vasomotor changes of which they may form part. Other organs which are not directly influenced to any appreciable extent by vasomotor nerves, as, for instance, the brain, do not actively swell and shrink; the passive variations—distension by high blood-pressure, collapse of volume with low blood-pressure—are on the contrary well-marked and uncomplicated effects. The spleen on the other hand varies in most complicated fashion; it is a very distensible organ and can therefore undergo considerable passive changes; it is abundantly supplied with vasomotor nerves, and has therefore a considerable range of active vascular variations of volume; and thirdly it is highly contractile by virtue of its framework of involuntary muscle, so that, independently of passive and vasomotor variations, it can rhythmically dilate and contract.

The most notable of Mosso's plethysmograph experiments is that intended to demonstrate a variation of cerebral circulation coincident with cerebral exertion; Mosso found that the volume of the arm was diminished during the performance of a calculation or other mental effort, and concluded that the effect was due to increased blood-supply to the brain; the results of the experiment are however not sufficiently regular to bear out this conclusion; alterations of volume of the arm, when they occur at all, are probably due to alterations of respiratory movements.

The *sphygmomanometer* is an instrument by means of which the pulse-tension can be approximately measured on man; the principle upon which it is based being the determination of the amount of counter-pressure which is just sufficient to extinguish the pulse. A simple form of the instrument is as follows: an elastic finger-stall distended with air and connected with a mercury manometer is squeezed down upon the radial artery until the pulse is felt to vanish beyond the point of compression (recurrent pulsation being if necessary eliminated by compression of the ulnar artery); the pressure of air within the finger-stall as indicated by the manometer now just exceeds the blood-pressure within the radial artery during cardiac systole.

The plethysmograph has also been employed for the same purpose, the principle of counter-pressure being utilised as follows: pressure of the fluid surrounding the limb (arm, hand, or finger) is raised until a point is reached at which the pulsatile alterations of volume are at a maximum; this point is taken to indicate when the pressure of fluid on the limb is above the intra-arterial blood-pressure during cardiac diastole, but below it during cardiac systole.

The pulse.—At each beat of the heart about four ounces of blood (or 120 c.c.) are forced by the left ventricle into the aorta and added to the mass of blood which is being pressed onwards throughout the arterial system. This sudden addition to the contents of an arterial system which is already distended, gives rise to a pressure wave throughout all the arteries of the body, called the arterial pulse, which can be felt in any superficial artery. The most readily accessible artery for this purpose is the radial; other accessible arteries are the temporal, carotid, axillary, brachial, femoral, popliteal, anterior and posterior tibials, in all of which the arterial pulse may be felt, and, if desired, examined by means of recording instruments. The practical value of the pulse is that it affords means of judging of the state of the circulation; counting the pulse is the readiest means of ascertaining the frequency of the heart's beats, and the careful study of the tension of the pulse affords valuable information regarding the state of the arteries; it enables us to judge whether the general arterial pressure is high or low or about normal. The normal *frequency* of the pulse (*i.e.* of the heart's beat) is about seventy per minute in the male, eighty per minute in the female, and still higher in children; in the fœtus before birth it is 130 to 140. The frequency is increased by exertion, by taking food, by alcoholic stimulants, by some forms of emotion, in fevers, and in all kinds of debilitating disease. It is diminished during rest, during sleep, in some forms of emotion, in cerebral coma. As regards emotion it is generally pleasurable and exciting emotion that raises the pulse-frequency, painful and depressing emotion that lowers it. As regards exertion, even the slight differences of exertion which insensibly accompany differences of posture affect the pulse-frequency; thus, for instance, in the same person the pulse has been counted in the lying posture 70, sitting 75, standing 80, and after a short run 120; in a weak or sick person the differences with posture may considerably exceed those observed in health; thus the difference in the sitting and lying postures may be twenty beats; it is therefore worth noting, when it is possible, what that difference is, for the number gives some measure of the weakness of the subject. Temperature also affects the pulse-frequency—high temperature raises it, low temperature lowers it; in the same person with a normal pulse frequency of 72 the pulse has been counted in the hot chamber of the Turkish bath 96 per minute, and in a cold bath 60 per minute.

The pulse may feel *large* or it may feel *small*; these terms signify that the impression is conveyed to the observer, of a large or of a small wave of blood passing under his fingers as they rest upon the artery; but the terms are apt to mislead, as will presently appear from other considerations. The same remark applies to the terms *strong* and *weak*, for an apparently 'strong' pulse is common when arterial pressure is low, an apparently 'weak' pulse when arterial pressure is high. It is more important to pay regard to the *compressibility* of the pulse, and to speak of the *hard* pulse or the *soft* pulse. A hard pulse is one which requires considerable pressure of the fingers upon the artery to obliterate; the artery feels distended between the beats, and the more the fingers compress it—within certain limits—the more forcible does the beat appear. A soft pulse is easily obliterated by compression and appears most forcible when the fingers are lightly applied. The hard pulse is a sign of high arterial tension or pressure, the soft pulse is a sign of low arterial pressure; generally speaking hard pulses are of lower frequency than soft pulses, and usually the hard pulse appears small and weak in comparison with the soft pulse if both are felt with a light touch. The terms *long* and *short* are sometimes used to signify that each beat appears to last under the finger for a long or a short period; they are unnecessary terms, for the long pulse is hard, the short pulse is soft. *Slow* and *quick* are sometimes used to mean the same as long and short respectively, and are equally unnecessary terms. *Rapid* and *slow* are occasionally employed to signify that the pulse is felt at a short or long interval after the heart's impulse. The supposed differences of the interval are imaginary; there is an interval, it is true, but the interval varies so little as to be quite inappreciable without the aid of delicate instruments.

From these remarks it appears that the characters of the pulse which can be recognised and named without ambiguity are (1) frequency, (2) compressibility. The pulse of high arterial tension is infrequent and hard (*rarus et durus*). The pulse of low arterial tension is frequent and soft, and sometimes palpably dicrotic (*frequens et mollis*). Every normal and most abnormal pulses are dicrotic in so far as their tracings reveal the presence of the dicrotic wave; clinically, however, the term *dicrotic pulse* is reserved for cases in which the wave is so marked as to be easily felt; a dicrotic pulse is a pulse of low tension, and when well marked gives to the finger of an observer a double tap with the rhythm of a postman's knock. An *intermittent* pulse occurs when, in otherwise regular series of heart beats, one or more beats are occasionally dropped; thus differing from an irregular pulse in which there are irregular intervals between the successive heart beats, and usually great variety of strength of beat. The pulse of aortic regurgitation is so strikingly characteristic as to call for separate mention. It is termed a 'collapsing' or 'water-hammer' pulse, and its character is due to the fact that an abnormally large ventricle drives an abnormally large quantity of blood into an arterial system which in consequence of backward escape through the aortic orifice does

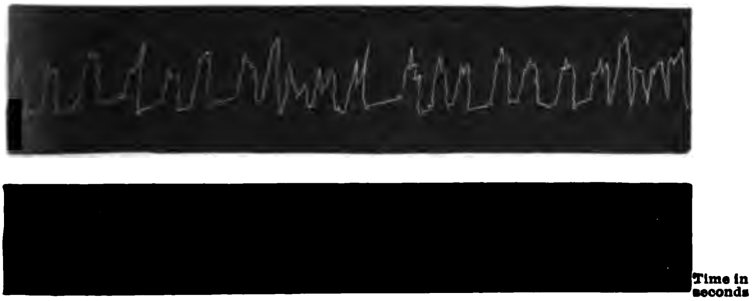


FIG. 38.

Tracings of an irregular palpitating heart due to excessive tobacco smoking (upper line), and of the same heart after administration of digitalis (lower line).

not remain properly filled between the beats. In the examination of pulse-tension by the radial artery a *recurrent* pulse may often be felt beyond the point where the vessel is completely compressed; such a pulse is due to free anastomosis with the ulnar artery and ceases when both radial and ulnar arteries are compressed. A *venous* pulse may occur under various conditions; physiologically it is produced when the arterioles are widely dilated so that the arterial pulse is propagated through them and through the capillaries into the veins; an instance of this kind of venous pulse occurs in the case of the submaxillary veins during excitation of the chorda tympani; it is also observable in the veins o the back of the hand after immersion in warm water. Anothe variety of venous pulse is the backward pulse observable in th jugular veins when from any cause the tricuspid orifice gape during systole. A *capillary* pulse can be brought into evidenc on most normal persons and with great distinctness in cases c aortic regurgitation; it is seen as a systolic flush of colour a the root of a finger nail or in a portion of skin soon after it ha been compressed.

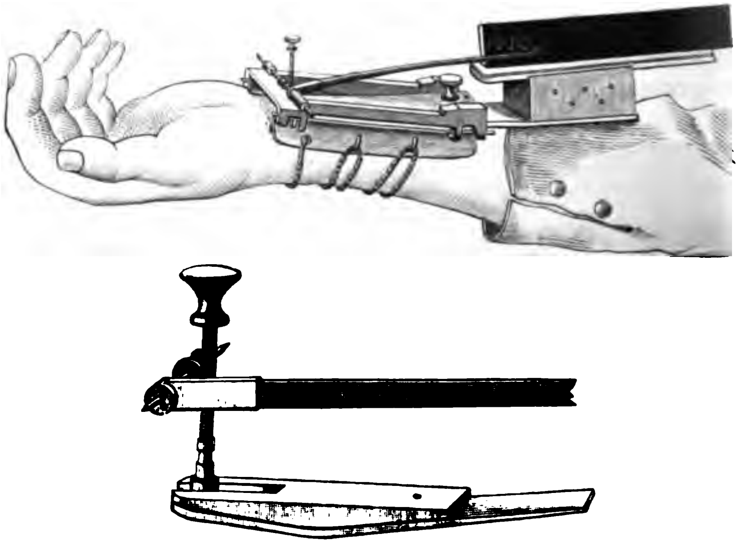


FIG. 39.

Marey's sphygmograph applied to the radial artery.
Portion of lever and spring which presses upon the artery.

The *sphygmograph.*—If a lever rests upon an artery such a the radial at the wrist, so as to compress but not obliterate it, each pulsation will visibly raise the lever. A lever arranged thus and marking its movements upon a travelling surface constitutes a *sphygmograph*.

The sphygmograph has proved useful as an instrument by which certain characters of the pulse have been demonstrated, but it has no valid claim to be regarded as furnishing any clinical information which is not furnished by a skilled touch. A knowledge of sphygmographic tracings gives greater definiteness and precision to the sensations obtained by feeling the pulse; on the other hand an unguarded use of the instrument, or too minute interpretation of tracings, to the exclusion of a due regard to the palpable character of the pulse, is very likely to mislead with false evidence. The instrument may, in fact, be an added source of error, and had better be avoided than carelessly used.

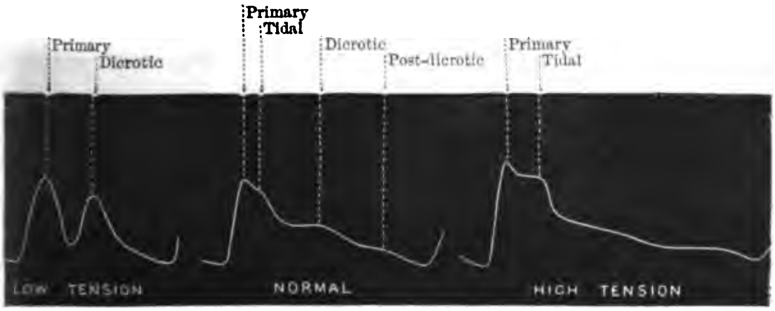


FIG. 40.

A normal pulse-tracing presents the following features: When the pulse wave reaches the artery where it is compressed by the lever, the compressed portion expands and the lever is raised, giving on the tracing the *primary* or *percussion* wave; the expansion of the artery having quickly reached its maximum begins to subside and the lever begins to fall; the decline is delayed by a brief period of maintained expansion which may amount to an actual wave of renewed expansion; this interruption of the decline or second rise, as the case may be, is called the *tidal* or *predicrotic* wave; the decline in the expansion of the artery now continues rapidly and the lever falls correspondingly until the decline is suddenly arrested and replaced by a distinct increase of expansion constituting the *dicrotic* wave; between the two chief waves—the tidal and the dicrotic—a more or less distinct depression is marked, which is sometimes spoken of as the dicrotic notch. Subsequently to the dicrotic wave, the expansion of the artery continues to decline, the regularity of the decline being sometimes interrupted by a fourth wavelet, called from its position the *post-dicrotic* wave.

Are all these waves truly the expression of the varying states of pressure within the artery, or are they in part or wholly due to instrumental oscillations? To this question, which has been much debated, we may answer at once that the percussion wave and the dicrotic wave are really caused by intra-arterial waves of pressure and consequent expansions of the compressed artery. If a horizontal jet from any small artery be received on a revolving drum covered with white paper, the blood marks a kind of pulse tracing on the paper: such a tracing shows two waves, the primary wave and the dicrotic wave. These waves are therefore certainly arterial and not instrumental. The post-dicrotic wave is inconsiderable, it is probably instrumental and it indicates nothing in particular. The predicrotic or tidal wave is, properly speaking, due to a state of maintained expansion, rather than to any separate wave of expansion; it is probably exaggerated by the sphygmograph, the lever of which is apt to rebound after its fall from the primary or percussion rise. But apart from this possible source of deformation the tidal wave or state of maintained arterial expansion has a real value as an index of arterial condition. Normally in the radial artery it is not very pronounced; in the brachial or in the carotid artery—*i.e.* nearer the heart—it is much more marked; abnormally, it may be a well-marked feature of the radial pulse curve, and is then a sign that arterial tension is high, or that the arteries are abnormally rigid; it is a constant feature of the radial pulse-tracing taken on old people, and if it is found on the pulse-tracings of people at or below middle age, it indicates

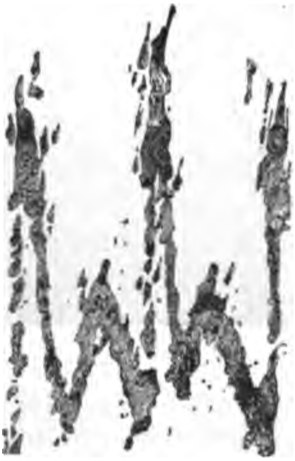


FIG. 41.—HÆMAUTOGRAM. (Landois.)

a prematurely 'aged' and rigid state of their arteries. Such a pulse would feel long and hard—*tardus et durus*; if due to high arterial tension it would be felt full between the beats, if due to rigid arteries it would be felt empty between the beats. When arterial tension is low, the tidal wave does not appear in the radial pulse-tracing, and may even be absent from the brachial tracing. The dicrotic wave is on the contrary exaggerated—so much so that the pulse can be felt to be double—whereas in high tension pulses it is very ill-marked. The low tension pulse is short and 'compressible' and feels empty between the beats—*celer et mollis.*

The nature of the dicrotic wave has been much disputed. Does it, like the percussion wave, travel from the heart towards the periphery; or is it a wave reflected from the periphery? It is probably the former, and produced as follows: when the systolic discharge commences, the primary pressure wave starts; while this discharge continues, the tidal pressure wave is maintained; when it suddenly ceases, a negative pressure wave starts which gives rise to the dicrotic depression; the semilunar valves now suddenly close and uphold the column of blood in the aorta; the cessation of the negative wave, and the sudden arrest of the column of blood by the semilunar valves together give rise to a second positive wave starting from the aorta and propagated throughout the arterial ramifications as the dicrotic wave. It is, however, not always easy to identify these so-called tidal and dicrotic waves on all kinds of tracings, nor may we assume that their mechanism is always the same; recent observations show that *reflected* waves may possibly occur in the arterial system of the dog (v. Frey).

Velocity of the pulse.—The cardiac impulse and the radial pulse are not absolutely synchronous, as may easily be verified by feeling the two impulses simultaneously—the radial pulse will be felt a short interval after the cardiac impulse; or if the heart be listened to while the radial pulse is felt, the latter will be noticed to occur after the first sound, about midway between the first and second sounds. Nor is the pulse simultaneous throughout the arterial system; for instance, the carotid may be felt to precede the radial pulse, and the femoral to precede the tibial pulse. In short the cardiac discharge gives a pulse throughout the arterial system propagated with a definite velocity from the heart to points further and further removed. This velocity is measurable by instruments by the method of simultaneous tracings taken on a revolving cylinder. If, for instance, the cardiac impulse and the radial pulse be simultaneously recorded by levers, the points of which are vertically beneath each other, it will be noticed that the cardiac lever begins to rise before the radial lever, and if the interval between these initial points be compared with a time tracing, as of a vibrating tuning-fork, its time-value may be determined with great accuracy. This interval is spoken of as the *pulse-delay*; it is as follows at different points of the arterial system in hundredths of a second.

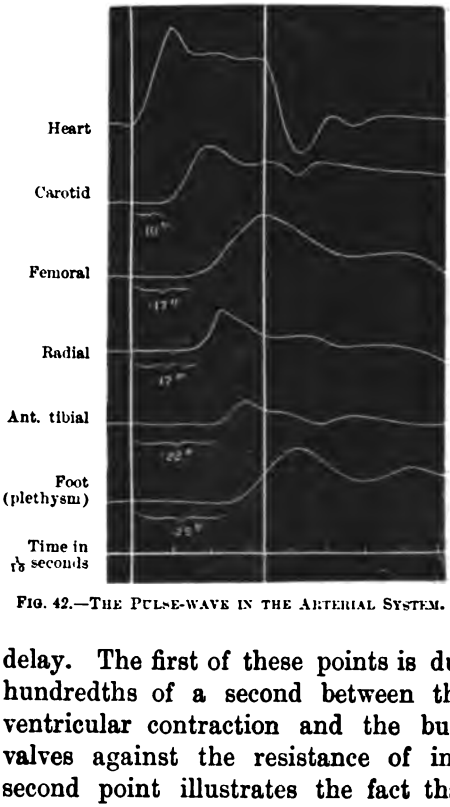


FIG. 42.—THE PULSE-WAVE IN THE ARTERIAL SYSTEM.

Heart-carotid	interval .	10
Heart-radial	„ .	17
Heart-femoral	„ .	17
Heart-tibial	„ .	22
Carotid-radial	„ .	7
Femoral-tibial	„ .	5

In these measurements it is to be noted, (1) that the heart-carotid delay is disproportionately long; (2) that the carotid-radial is longer than the femoral-tibial delay. The first of these points is due to an interval of 6 to 8 hundredths of a second between the commencement of the ventricular contraction and the bursting open of the aortic valves against the resistance of intra-aortic pressure. The second point illustrates the fact that the pulse-wave travels more rapidly in the arteries of the lower than in those of the upper extremity. The average velocity of the pulse-wave is 9 meters per second; this velocity must not be confused with the velocity of the blood-current, which does not exceed ·3 meter per second. The velocity of the pulse wave is a very constant magnitude; variations of velocity are comparatively small and not to be detected by feeling the pulse. Clinically a 'delayed' pulse is usually a weak pulse, or a pulse is erroneously called 'delayed' because it is timed with reference to a diastolic instead of a systolic impulse. The radial pulse never succeeds the second sound of the heart, even when the systole is at its shortest; normally it is felt to be equidistant between the first and the second sound.

On the properties and mode of contraction of cardiac muscle.—The normal heart contracts regularly; the same heart removed from the body and empty of blood, continues for a time to contract regularly—on warm-blooded animals for a few minutes, on cold-blooded animals for several hours. The heart thus differs from all other muscles, which do not contract until they are stimulated, and possesses within itself the conditions of regular and apparently spontaneous action. What are these conditions and by what portion of the heart's substance are they possessed? In other words, what is the cause of the heart's rhythm? Various answers have been given, different theories have been proposed, and the study of the question has brought many facts to light. These we have to consider. It has been answered that the continuance of the rhythmic beat is owing to the presence of ganglia; a theory has been advanced to the effect that these ganglia rhythmically discharge themselves, and thus excite rhythmical contraction of the muscle. This theory was based upon the observation of the fact (?) that on cold-blooded animals, not only the entire organ, but separate bits will continue to beat for a time; on microscopic examination ganglia were found in such bits, while in other bits which remained motionless ganglia were sought for in vain. Such observations are liable to vary with the expectation of the observer, and they are contradicted by exactly opposite observations; the lower two-thirds of the frog's ventricle—a so-called *ventricle-apex* preparation—which contains no ganglia, will, if supplied with nutrient fluid, continue to beat rhythmically; a strip of muscle cut from the ventricle of the tortoise, and destitute of ganglia, may after a longer or shorter period of quiescence commence and continue to beat. These last observations are accepted as correct, and ganglia are not now believed to be essential to the continuance of the heart's beat. The property of rhythmic contractility is an attribute of cardiac muscle, and it is useless to ask what the cause of that property is; all that may be said is that the power of rhythmically beating belongs to cardiac muscle while it is alive, whether in the body or out of the body. Another theory may be mentioned but only to be dismissed as unfounded. Brücke thought that the rhythmic alternation of action and rest was owing to a rhythmic mode of nutrition; he thought that this was affected by a peculiarity in the blood-supply by the coronary arteries, he imagined that these were shut off from the aorta by its semilunar valves during the systolic discharge, but flushed with blood during the diastole, and he supposed that the diastolic blood-supply and consequent nutrition constitute the cause of each systolic contraction. This theory is quite untenable, it does not account for the action of the excised heart or of the frog's heart or of bits of heart; the supposition that the coronary blood-supply occurs during diastole is not even correct—the arterial pulse is systolic in the coronary as in all other arteries. Nor does the heart stop at once after the complete arrest of circulation through the substance of its muscle by ligature of the coronary arteries; it continues to beat for several minutes after this operation, which is indeed equivalent in its effects to the actual excision of the organ.

Stannius' experiments.—At a period when the attention of physiologists was focussed upon the ganglia of the heart and their supposed mode of action (1852), Stannius made certain experiments upon the excised frog's heart which have been constantly referred to by subsequent observers and explained in many different ways. Apart from their explanation, which cannot be given as settled, which, indeed, is even more obscure since we have become assured that rhythmic contractility is a property of cardiac muscle *sine* ganglia, the chief facts observed by Stannius were as follows: if a ligature be tightly applied round the heart at the junction of the sinus with the auricle the auricle and ventricle stand still in diastole while the sinus continues to beat. If now a second ligature be applied round the heart at the junction of the auricle with the ventricle the ventricle recommences to beat, quickly at first, but gradually more slowly, while the auricle remains quiescent. The quiescent state of the auricle and ventricle consequent upon the first Stannius ligature closely resembles the state consequent upon vagus stimulation, the arrest being in diastole and the heart remaining capable of contracting in response to mechanical or electrical stimuli. But that the arrest is not, as might be supposed, due to vagus excitation by the ligature, i proved by the fact that the standstill is equally effected by ligature after atropin poisoning, which completely abolishes vagus excitability. The effects of the first and second ligatures have been 'explained' as follows. Ganglia are present (1) in the sinus (Remak's ganglion), (2) in the auricle (v. Bezold's ganglion), (3) at the base of the ventricle (Bidder's ganglion). It has been supposed that 1 and 3 are 'motor,' and 2 'inhibitory'; that the motor influence of 1 and 3 combined is greater than the inhibitory influence of 2, consequently in the absence of all ligature the heart beats; that the motor influence of 3 is less than the inhibitory influence of 2, consequently after the first ligature, cutting off the motor influence of 1, the auricle-ventricle stands still; while after the second ligature, cutting off also the inhibitory influence of 2, the ventricle influenced by 3 alone and unopposed, recommences to beat. Obviously such an 'explanation' explains nothing, and only translates Stannius' facts into other and very doubtful terms which add nothing to our knowledge. It is preferable to remember the facts as they stand, without attempting to assign to them a significance which cannot be proved.

We are, indeed, beginning to modify our statements of the facts themselves. The standstill after the first ligature is not permanent nor even of long duration; half an hour is a comparatively long period for it to last—more usually its duration is only a few minutes, at the expiration of which the auricle-ventricle recommences to beat; sometimes the ligature fails entirely and the auricle-ventricle goes on beating, slowly at first and gradually faster. Again, a ligature in the auriculo-ventricular groove may cause the ventricle of a quiescent auricle-ventricle to resume its beat as above stated, but it may also temporarily arrest the beat of an actively beating auricle-ventricle. It appears rather as if the property of rhythmic contraction possessed by all parts is at its maximum in the sinus, at its minimum in the ventricle, while in the ventricle it is greater at the base than at the apex; contraction normally starts from the point of greatest instability, *i.e.* from the sinus; removal of the sinus removes a leading part and causes shock, and the beat of the rest of the heart ceases for a period; after a time the beat recommences, contraction starting from the auricle; a second ligature or section removing the auricle may cause a similar result, viz. a temporary cessation of the ventricular beat, or if (omitting the ligature at the sinus-auricle junction) a ligature be at once applied to the auriculo-ventricular groove, the ventricle will be temporarily arrested in diastole. In short, though usually the first ligature gives arrest which is ended by the second ligature, yet under varied conditions the first ligature may fail to give arrest, or the second ligature may give arrest. The results are thus not only complex, but variable, and cannot be made to bear any precise significance. No corresponding results have been obtained on the mammalian heart; if all nervous communication between the auricles and ventricles be destroyed, the chambers continue to beat, but with independent rhythms; vagus stimulation now fails to arrest the ventricles, while it still produces auricular standstill.

'All or Nothing.'—But if the theoretical significance of Stannius' experiments is obscure or doubtful, it is otherwise as regards their practical value. The first Stannius ligature affords a constantly employed means of obtaining the frog's heart in a quiescent state, when it can be excited and employed for experiments which could not be made while it is spontaneously beating. If a 'stanniused' and consequently quiescent frog's heart be subjected to stimuli of gradually increasing strength, it is found that th weakest stimulus which produces any effect at all, produces all th effect of which the muscle is capable, in other words the effect i at once a maximum effect; a single stimulus either produces n effect at all, or it produces the full effect of which the muscle i capable; '*all or nothing*' is the motto of the heart's contractio under these circumstances. To what extent may we suppose tha this holds good for the normal beat? Do a succession of norma systola vary in strength, or are they uniform and maximal The usual answer is that they are normally maximal and complete, and that the ventricle normally empties itself of its conten completely, but it is obvious that this does not imply equality i successive contractions, for the successive charges vary i amount, being greater or smaller and consequently expelled b greater or smaller contractions; still the motto, 'all or nothing holds good, the contraction whether great or small is th greatest possible, *i.e.* maximal, and the normally acting ventric is completely emptied at each such contraction. Abortive o incomplete contractions are abnormal.

The staircase.—A stanniused heart, excited at regular interva of say two seconds by single induction shocks sufficiently stron to make the heart beat without fail, gives a succession of contractions of increasing magnitude. Each contraction, although 'maximal' inasmuch as it is the full effect of which the muscle is then capable, is a little greater than the preceding contraction, and the general outline of such a series when recorded is that of a staircase, each ascent of the recording lever from the base line reaching a step higher than its predecessor (Bowditch).

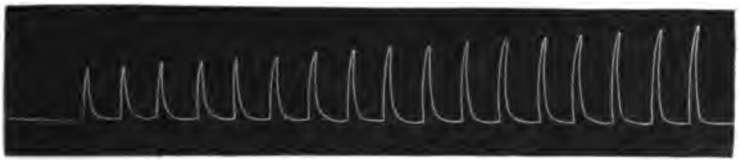


FIG. 43.

'Staircase' of beats of a stanniused frog's heart excited by maximal induction shocks at intervals of three seconds.

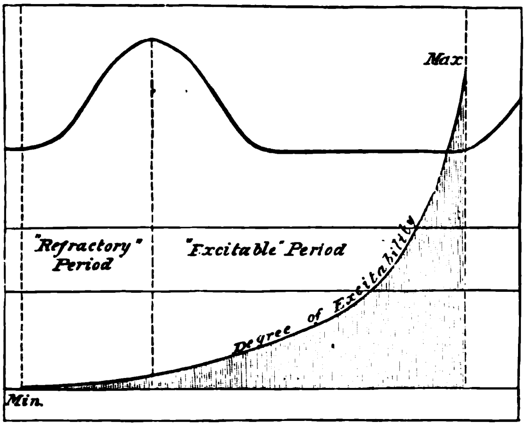


FIG. 44.

To illustrate the varying excitability of a frog's heart at different periods of systole and of diastole. The excitability is lowest during the first half of systole, greatest during the second half of diastole.

The effect is not, however, peculiar to cardiac muscle; ordinary voluntary muscle stimulated by a succession of maximal induction shocks usually gives an ascending or staircase group before entering upon the decline due to fatigue.

The refractory period; tetanus.—The heart is not equally excitable during rest and during action; it is less excitable during action than during rest, further it is less excitable during rising action than during declining action, *i.e.* during the beginning than during the end of systole; the comparative inexcitability is so marked during the commencement of systole that this period has been termed the *refractory period.* These variations of excitability are not absolute but relative, the heart is not absolutely inexcitable during systole, but only less excitable than during diastole. Further the inexcitability is more profound during earlier than during later portions of the systolic period, and a similar statement holds good for the other periods, the state of excitability being at its minimum at first, thence progressively increasing to its maximum, when a second spontaneous beat is about to be discharged (*v.* Fig. 44). Similar statements are applicable to excited beats of the stanniused heart.

Can cardiac muscle be *tetanised* like voluntary muscle by a rapid succession of stimuli? To this the experimental answer is '*No,*' as might be foreseen from consideration of the refractory period. The early stage of each excited contraction is refractory to stimuli, which consequently fail; the refractory state is not absolute, but shorter and shorter to increasing strength of stimulus. Strong rapid stimuli can consequently increase the rapidity of the beat, and to such an extent as to give an incomplete tetanus, but complete uniform tetanus like that of voluntary muscle cannot be obtained by a succession of stimuli.

The wave of contraction.—A contraction, whether spontaneous or excited, is not absolutely simultaneous throughout the whole mass of the ventricle, but it sweeps over the contractile tissue from its seat of origin. This is easily verified by simultaneou tracings of two levers resting on different parts of the ventricle these do not rise together, but one after the other. A stanniused and therefore quiescent frog's heart thus treated shows that th *wave of contraction* can travel in either direction from apex to base or from base to apex, according as the ventricle is stimulated at th apex or at the base. A strip of muscle cut from a freshly excise mammalian heart, placed beneath two levers will contract wave like from either end to the other, raising one lever after the other according to the end which is stimulated. This wave-like progress of contraction occurs also in the natural beat; in the frog's ventricle it is from base to apex; the velocity of the wave can b calculated, *e.g.* if the two levers are 1 cm. apart, and the tim interval between the initial points of their elevation $\frac{1}{10}$ sec., the velocity must be 10 cm. per sec.

In the mammalian ventricle it is far more difficult to obtain evidence of the passage of a wave of contraction, unless the rapidity of movement has been reduced by cooling. In the normal beat of the warm-blooded heart it is impossible to tell by mechanical means whether the contraction begins at the apex or at the base. The only other means of exploration is afforded by electrical instruments; we shall find, when we come to speak of these, that the test can be applied to the unexposed as well as to the exposed heart, but we may state now that in the second case we have no assurance that the organ continues to beat normally, while in the first the indications are difficult to decipher with certainty. Any dogmatic statement concerning origin, course, and speed of the wave would therefore be out of place here.

'*Blocking.*'—If a strip of heart muscle which is still excitable be compressed between two levers resting upon it, and stimulated at one end, the contraction recorded by the lever beyond the point of compression is delayed or may be abolished; the passage of the stimulus is more or less *blocked*. If a frog's heart is set up between the jaws of a clamp which just holds it at the auriculo-ventricular junction, it will while fresh give a series of auricular followed by ventricular contractions. If the clamp be tightened it may give only one ventricular for every two or more auricular contractions. Compression has blocked the passage of stimuli from auricle to ventricle, and instead of every stimulus fulfilling its effect, every other or every third stimulus is alone effectual in consequence of partial 'blocking' at the compressed auriculo-ventricular junction (Gaskell).

Drugs by which the action and properties of the heart can be modified.—Many different drugs modify the heart's action, the effects produced being in certain cases marked and predominant, in others appearing as subordinate features among effects better characterised elsewhere than upon the heart. It is not possible to draw up an accurately classified list of cardiac drugs under definite headings such as 'cardiac stimulants,' 'cardiac sedatives,' &c.; it is better to take each drug separately and describe its best characterised effects upon the heart, such as alterations of the spontaneous beats, of the excitability, and of the tone of cardiac muscle, or modifications in the excitability of its nerves. We shall find that theories as to the exact parts affected by different drugs are numerous and ingenious, but we shall endeavour to keep these theories very distinct from the tangible facts, and to avoid the description of experimental results in language involving theoretical assumptions. For example, the statement that 'muscarin stops the heart in diastole, atropin sets the heart beating again,' is simply descriptive of evident effects, whereas the statements 'muscarin excites inhibitory ganglia, atropin paralyses them,' or 'muscarin paralyses motor ganglia, atropin excites them,' include suppositions which may or may not be true. The apparently simple proposition 'muscarin excites inhibitory ganglia' is in reality composed of the descriptive statement 'muscarin stops the heart,' and of the more or less probable suppositions that the heart is stopped by inhibitory ganglia, and that muscarin has a specific action upon inhibitory ganglia. We may take this opportunity of formally recognising a distinction which is of universal value, and especially desirable in physiological study. Descriptive statements are definite and open to proof or disproof; inferential statements are liable to be indefinite and impregnable by proof or disproof; composite statements involving in the same words description and interpretation are treacherous and embarrassing. A descriptive statement applies to matter of fact and must always be of intrinsic value, although it may be o more or less importance. An inferential statement convey explanation of admitted fact, and is sometimes of the utmos value, but it is dangerous and liable to abuse. A mixed statement is useless or mischievous, and should, whenever possible be decomposed into its positive and suppositive components 'Muscarin excites inhibitory ganglia' is a mixed statement 'Muscarin stops the heart' is a positive statement. 'Inhibitor ganglia stop the heart'—'Muscarin acts upon inhibitor ganglia,' are suppositive statements.

The chief drugs of which the action upon the heart has bee most carefully studied in the laboratory are:—*muscarin, pilocarpin, atropin, nicotin, physostigmin, curare, digitalin, aconitin, veratrin; acids, alkalies,* and *neutral salts; alcohol, chloroform,* and *ethe* Of these drugs, *atropin* and *muscarin* are of most interest from physiological standpoint, while their use as cardiac medicines i very limited; on the other hand digitalis, aconite, ether, &c., ar of far more importance as therapeutic agents, and this has le to their exhaustive examination in the laboratory.

Muscarin is an alkaloid extracted from a poisonous mushroom —amanita muscaria—present also in putrefying fish or flesh. The effect of a small dose of muscarin injected into the circulation of a dog or rabbit, or directly applied to the exposed heart of a frog, is a rapid diminution of the heart's beat, ending in its complete arrest in diastole. This state closely resembles that of a heart arrested by vagus stimulation, the muscular substance of the heart remaining responsive to direct stimulation. The generally received *theory* is that muscarin strongly stimulates inhibitory ganglia of the heart, and that to a less degree it exercises a direct effect upon the cardiac muscle itself, depressing its excitability.

Pilocarpin has an action on the heart similar to that of muscarin.

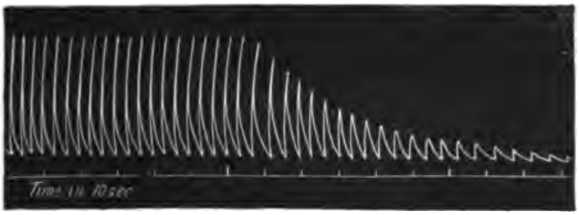


FIG. 45.—EFFECT OF MUSCARIN UPON FROG'S HEART.

Atropin.—A small dose of atropin injected into the circulation gives rise to a great increase of pulse-frequency; the effect is similar to that consequent upon section of the vagi; the atropin effect is correspondingly well-marked on dogs, ill-marked upon rabbits. Excitation of the vagus on atropinised animals fails to slow or arrest the heart's action. Thus the effect of atropin is equivalent to an interruption between vagus and heart, and the *theory* given is that atropin paralyses the intracardiac inhibitory apparatus. On frogs atropin directly applied to the exposed heart gives no appreciable alteration of the beat, but excitation of the vagus or of the sinus-auricle junction fails to arrest the heart—if anything quickens it owing to excitation of accelerator fibres. A heart in diastolic arrest as an effect of the application of muscarin recommences to beat shortly after the application of atropin. Atropin is thus *antagonistic* to muscarin.

Nicotine, like atropin, abolishes the inhibitory effects of vagus stimulation; stimulation of the vagus of a frog poisoned with nicotine, so far from arresting the heart, actually accelerates it.

Physostigmin or *Eserin*, one of the alkaloids extracted from the calabar bean, in small doses increases the excitability of the vagus; it is in this respect to a limited degree an antagonist to atropin; a frog atropinised to a point when excitation of the vagus fails to arrest the heart, may recover its susceptibility to vagus stimulation after a small dose of physostigmin. After large doses of physostigmin vagus excitation fails to arrest the heart.

Curare, which acts more particularly on the termination of nerve in voluntary muscle, may also if administered to excess interfere with the action of the vagus on the heart. On fully curarised frogs vagus excitation consequently fails to arrest the heart.

Digitalin, the chief alkaloid of digitalis, at first exaggerates the excitability of the vagus or actually excites it; the signs of this are that unusually weak stimuli will arrest the heart, or that the frequency of the beat is actually lowered. As a later effect the excitability of the muscle itself is increased, the sign of this being prolonged and stronger systolic contraction, so prolonged as to merit the name of cardiac contracture. The progressive effects of digitalin upon the heart may be grouped as follows:—1*st stage*. Increased strength, increased duration and diminished frequency of the heart's beat; 2*nd stage*. Irregular, often dicrotic and frequent beat; 3*rd stage*. Systolic arrest; *post mortem* the heart of frogs is usually found in systole, of dogs sometimes in systole, sometimes in diastole. Medicinally digitalis is classed as a cardiac tonic.

Veratrin has an action on the heart similar to that of digitalis. The prolongation of the contraction is even more marked; it is abolished by potassium chloride.

Aconitin, like digitalis and veratrin, excites the vagus and slows the heart; on frogs the slowing is preceded by a short stage during which the beat is more frequent; on dogs and on man this is not the case, the heart's beat becoming slower from the beginning. Medicinally aconitin is classed as a cardiac sedative.

Alcohol, chloroform, and ether, in small doses, are cardiac stimulants, causing the heart to beat more rapidly and more strongly. In larger doses they become depressant.

Acids and alkalis, in dilute solution, affect the duration of the systole and the tone of the heart. Dilute alkali (caustic potash $\frac{1}{20,000}$) prolongs the systole, and leads to tonic contraction in systole Dilute acid (lactic acid, $\frac{1}{20,000}$) shortens the systole and weaken it, leading to complete relaxation and arrest in diastole. These statements refer to the frog's heart, through which solutions are made to circulate.

Neutral salts.—A solution of sodium chloride in distilled water, ·6 per cent. made to circulate through the frog's heart, has no power of maintaining the beats; these gradually and progressively decline. The addition of a minute trace of calcium chloride restores the beats and causes them to become prolonged. The further addition of a trace of potassium chloride causes these prolonged beats to resume their normal character. Thus $NaCl$, $CaCl_2$, and KCl in dilute solution compose a fluid which maintains normal beats of the heart better than the solution of any one, or any two, of these salts alone; such a fluid may therefore be termed a '*nutritive*' fluid (Ringer).

'*Nutritive*' *fluids.*—The nutritive quality of such a fluid may be improved by the addition of a minute trace of serum-albumin, or of a solution of serum-ash, or of milk, or blood, or blood-serum. When any of these fluids are made to circulate through the frog's heart, it may continue to beat normally for many hours, and the modifying influence of drugs can be conveniently observed by adding them to the nutritive fluid. Egg-albumin, albumose, and peptone have no nutritive action upon the heart, or even a contrary effect; the only proteid possessing a true nutritive action is serum-albumin (Kronecker).

Perfusion-cannula and frog-heart apparatus.—Many of the results enumerated above, in so far as they relate to the behaviour of the frog's heart, have been obtained by means of an apparatus permitting a record of the contractions to be taken while solutions of different substances are made to flow through the heart. The frog-heart apparatus in most general use are those of Roy and of Kronecker; in both the essential portion is the two-way or perfusion-cannula, which is introduced through the sinus venosus and auricles into the ventricle, and tied in so as to serve as the sole inlet or outlet; in Kronecker's apparatus the movements of the heart are recorded by a mercurial manometer, in Roy's the heart works in a vessel full of oil fitted up on the principle of the oncograph. To test the nutritive action of a fluid, the proceeding is as follows:—The heart is first to be 'washed out' by letting a stream of normal saline flow through the perfusion-cannula and heart until the spontaneous beats and the electrical excitability have disappeared; the test solution is now allowed to flow through the heart, and is known to be 'nutritive' or not, accordingly as electrical excitability and spontaneous contractions are or are not restored.

Physiological anatomy of cardiac nerves.—The cardiac nerves are formed by fibres derived from (1) the vagus, (2) the sympathetic. Both sets of fibres are efferent in function; the former restraining, the latter stimulating, the activity of the heart. A third set of fibres have been experimentally demonstrated in mammalia (cat, dog, rabbit), afferent in function, named *depressor*, on account of their influence upon the blood-pressure, and taking a somewhat variable course in the vagus or in its branches.

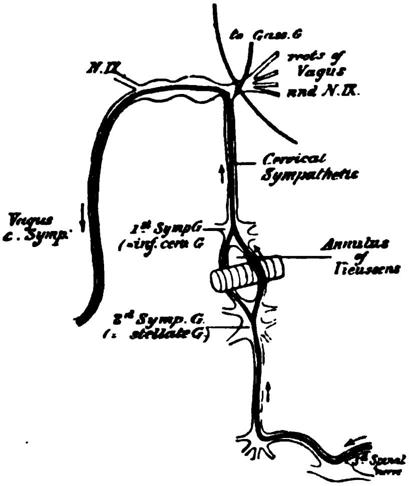


FIG. 46.—CARDIAC NERVES OF FROG (Foster).

Frog.—The vagus in the frog is in reality composed of two nerves, (1) the vagus proper, which is purely *inhibitory*, (2) a sympathetic branch which is purely *augmentor* of cardiac activity. The vagus proper has its origin or centre in the medulla oblongata, and after emerging from the jugular foramen is joined by a branch of the sympathetic derived from the spinal cord by way of a communicating branch from the third cervical nerve to certain sympathetic ganglia which may be regarded as analogous with the inferior cervical and first thoracic ganglia of mammalia (Gaskell). The conjoint vago-accelerans passes along the superior vena cava to the sinus venosus, thence along the auricular septum to the auriculo-ventricular ganglia.

Mammalia.—The cardiac nerves of mammalia (cat, dog, rabbit) comprise (1) inhibitory fibres to the heart, (2) accelerator fibres to the heart, (3) depressor fibres from the heart. The *inhibitory* fibres are derived from the spinal bulb by the internal branch of the spinal accessory; they run downwards in the vagus nerve and reach the heart by its cardiac branches. The *accelerator* fibres have their origin in the spinal cord; leaving it by the anterior roots of the second and third thoracic nerves, they reach the sympathetic by the white rami communicantes of these two nerves, and pass upwards through the first thoracic or stellate ganglion, annulus of Vieussens, and inferior cervical ganglion, from which they reach the heart through the cardiac nerves in company with the cardiac fibres of the vagus. The *depressor* fibres have their origin in the heart, pass along its cardiac nerves or (in the cat and rabbit) as a definite nerve which can be anatomically as well as experimentally isolated, join the superior laryngeal and vagus and thus reach the spinal bulb. As regards the minute anatomy of these fibres, it has been shown by Gaskell that the cardio-inhibitory fibres are small medullated fibres throughout their course in the spinal accessory, vagus and cardiac nerves, and probably remain medullated down to the cardiac ganglia. Cardio-accelerator fibres are small medullated fibres in the anterior roots, rami communicantes, and sympathetic channels up to the stellate and inferior cervical ganglia. From this point onwards in the cardiac nerves they are non-medullated.

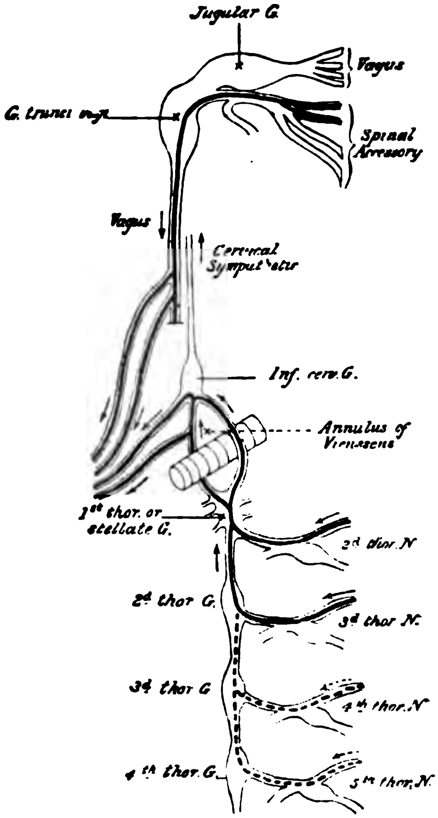


FIG. 47.—CARDIAC NERVES OF DOG (Foster).

Physiological anatomy of vaso-motor nerves. — The vaso-constrictor nerves of the whole body leave the spinal cord by the anterior roots of the thoracic nerves and enter the sympathetic system by white rami communicantes—in the dog by the sixteen pairs of nerves from the second thoracic to the fourth lumbar (Gaskell). The rami communicantes of the upper thoracic nerves pass to the cervical ganglia and form the cervical sympathetic; they also furnish the vaso-constrictor nerves of the anterior extremities by filaments which pass from the stellate ganglion to the brachial plexus. The lower thoracic nerves give off rami communicantes which form part of the abdominal splanchnic nerves, and furnish the vaso-constrictor nerves of the posterior extremities. The course of vaso-dilatator fibres is far more doubtful, owing to the fact that their presence at any given point is difficult of demonstration; all we may say with certainty is that, like vaso-constrictors, they take origin from the spinal cord and emerge by anterior nerve-roots. It is probable—and the probability is supported by experiments on the circulation of muscle—that dilating may be as widely distributed as constricting nerves, but their actually ascertained existence is practically limited to nerves of the head and of the pelvis (chorda tympani and nervi erigentes); and although we shall have occasion to refer to vaso-dilatation caused by the excitation of the sciatic and of the splanchnic nerves, we shall find that the facts themselves are not sufficiently assured to justify anatomical descriptions. According to Gaskell, however, vaso-motor nerves are microscopically distinguishable from spinal nerves, and the two kinds of vaso-motor nerves are distinguishable from each other; both kinds of vaso-motor nerve-fibres are of the small medullated kind (from $1{\cdot}8\mu$ to $3{\cdot}6\mu$ in diameter) and leave the cord in the anterior nerve-roots; but whereas vaso-constrictors pass from the spinal nerves to the sympathetic chain by white rami communicantes, and having lost their medullary sheath in a proximal series of ganglia (*i.e.* those composing the main sympathetic chain in the thorax and abdomen), return to the mixed nerve by grey rami communicantes, vaso-dilatators keep in company with the spinal nerves and remain medullated until they reach a distal series of ganglia (*i.e.* the prevertebral lumbar and sacral ganglia in the pelvis and the submaxillary ganglion on the chorda tympani). Thus from an anatomical as well as from a physiological point of view cardiac and arterial nerves may be classed in two groups, (1) vaso-constrictor and cardio-accelerator, (2) vaso-dilatator and cardio-inhibitory. Nerves of the first group, composed of fine non-medullated fibres, excite muscular action; nerves of the second group, composed of fine medullated fibres, restrain muscular action. On speculative grounds nerves of the first group are characterised as 'katabolic,' nerves of the second group as 'anabolic' (*vide* p. 104).

Physiological action of cardiac and vascular nerves.—The heart can beat independently of the central nervous system, but it is nevertheless subject to and controlled by nervous influences transmitted from the spinal bulb and cord by the vagus and sympathetic nerves. Similarly, the vessels—especially the small arteries—are subject to nervous influences transmitted from the bulb and cord by the sympathetic nerves. In each case these influences may either stimulate or restrain the contraction of the heart and of the arteries. To the heart the vagus or pneumogastric nerve is the channel of restraining or inhibitory influence, the accelerator nerves are the channels of stimulating or accelerator influence. To the vessels the sympathetic nerves are channels of influences which increase as well as of influences which diminish their contraction—of constricting as well as of dilating influences. It is by these nerves that the circulation is regulated; the cardiac nerves modify the beat of the heart, the vaso-motor nerves modify the state of the peripheral arterioles, causing the general and local alterations of blood-pressure and of blood-flow which have been described above (p. 59).

The Vagus; *effect of division.*—If one vagus be exposed and divided—on a dog, for instance—the heart's action undergoes little change; if anything, its beat may be somewhat more frequent than before the operation. If the other vagus be divided, the frequency of the heart-beat will be much increased—in some cases up to twice or three times that observed before the operation (on the dog; the effect is less marked on the rabbit). These facts show that the vagi are channels of a constantly exerted restraining or inhibitory influence which checks the action of the heart; when this restraint is abolished by section of both vagi, the heart beats on with greater frequency.

Effects of excitation.—If the peripheral end of one of the divided vagi be stimulated by induction currents, the frequency of the beat will be reduced to or below the normal according to the strength of stimulation; or, if the latter be sufficiently strong, the beat will be prevented altogether, and the heart will 'stand still' in a state of diastole. Division of the vagi lets the heart go, their stimulation holds the heart in. The vagus has thus a precisely opposite action to that possessed by the motor nerves of muscles; it does not excite but restrains cardiac contraction—it is an *inhibitory* nerve.

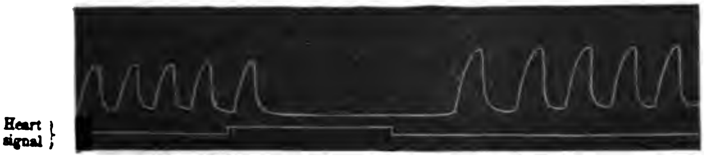


FIG. 48.

Effect of vagus excitation upon contractions of frog's heart; the time of excitation is indicated by the rise and fall of the signal line.

Does the vagus communicate directly with the cardiac muscle, or only indirectly by the intermediation of ganglia? Or, to put the question otherwise, does the vagus directly interfere with the action of the muscle, or does it interfere with the motor action of peripheral ganglionic organs? No assured answer can be given to the question. Upon the known fact that the action of the vagus diminishes the frequency and force of the beat, the opinion has been based that the vagus terminates in the muscle as well as in the ganglia, diminution of frequency being regarded as the sign of vagus action upon the ganglia, diminution of force as the sign of vagus action upon the muscle.

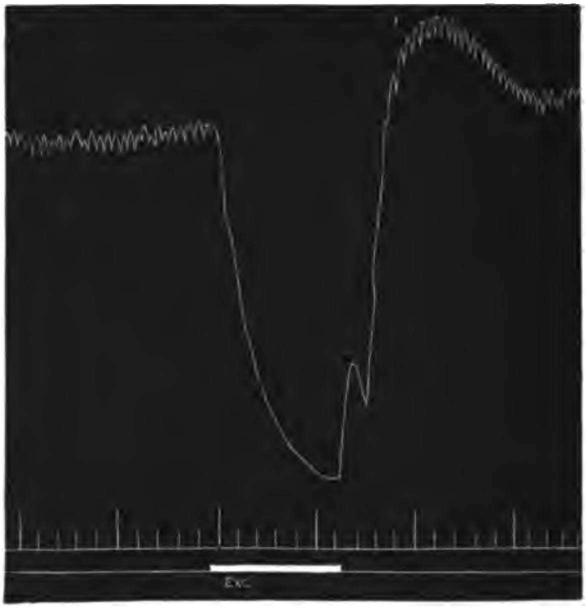


Fig. 49.

Blood-pressure tracing from a rabbit. Excitation of the peripheral end of the right vagus; fall of blood-pressure due to arrest of heart.

The effect of vagus stimulation is not produced immediately, but a short period elapses between the moment of stimulation and the consequent arrest. This *latent period,* which it is obviously impossible to estimate exactly (Donders roughly estimated it at ·05 second on the rabbit), is usually of such length that at least one heart-beat occurs after the commencement of stimulation.

The effect of vagus stimulation, applied for a short period, does not cease immediately with cessation of stimulation, but outlasts it, and is then termed the '*after-effect*'; the most typical vagus after-effect is a continuation of arrest followed by gradual recovery to and beyond the normal. Prolonged stimulation of the vagus is incapable of keeping the heart arrested for an indefinite period, although normally the vagus is in constant untiring action; the heart recommences to beat during the vagus stimulation, and may even beat more strongly than before.

If stimulation of one vagus is kept up until the vagus arrest has come to an end, stimulation of the second vagus will stop the heart. It must, however, be borne in mind that the two vagi are not always equal in their power over the heart; the vagus of the right side is commonly more effectual than that of the left side, though sometimes the case is reversed, and sometimes there is no observable difference.

The short duration of the effects of vagus stimulation is perhaps in part due to the comparative coarseness of experimental stimulation; but it is, doubtless, also due to the presence in the vagus nerve of accelerator fibres which come into action as the action of the true vagus wears off. Such accelerator fibres have recently been anatomically defined in the frog's vagus. Gaskell has isolated and stimulated, on the one hand accelerator filaments, on the other hand the vagus *minus* such accelerator filaments, obtaining in the first place acceleration, in the second case prolonged arrest of the heart—far more prolonged than can be obtained by stimulating the intact mixed vagus. Accelerator fibres have not been anatomically defined in the mammalian vagus, but experimentally their existence is, if not proved, made highly probable. The *typical effects* of moderate vagus stimulation are diminished force and diminished frequency of the beats of auricle as well as of ventricle, followed by increased force and increased frequency; *exceptionally*, there is no primary diminution, but an immediate increase of force and of frequency. It is therefore probable that the vagus contains at least two kinds of cardiac fibres—inhibitors, which give the typical effects; accelerators, which give the exceptional effects. But it must be recognised as a possible alternative or additional supposition that the differences of effect may be dependent upon a single kind of nerve-fibres having different effects according to the state of the heart and of its nerves. Excitation of a fresh vagus with a vigorous heart gives the typical inhibitory effects; excitation of a fatigued or otherwise depressed vagus with a sluggish heart is more apt to give the exceptional effects—primary augmentation and acceleration of the beat. Direct faradisation of the normally beating heart usually gives inhibition; direct faradisation of a moribund heart, which has almost or just ceased to beat, temporarily restores the rhythmic beat. These opposite effects may be ascribed to different nerve influences, or to different states of the same neuro-muscular apparatus. In favour of the first explanation we have the demonstration of separate inhibitory and accelerator nerves; in favour of the second, the fact that in hearts possessing no nerves (snails), direct faradisation may either arrest the beat or restore it.

On mammalia the inhibitory fibres of the vagus are derived from the *spinal accessory* by its internal branch; if the spinal accessory be torn out by the roots and its fibres allowed to degenerate, excitation of the vagus will no longer produce cardiac inhibition (Waller, 1856). The inhibitory effects of the vagus can be brought about *on man* by mechanical compression of the nerve; on criminals they have been obtained by electrical excitation of the vagus immediately after decapitation. The vagus continues to possess influence over the heart (both auricle and ventricle) of mammalia, for as long as the organ continues to beat after death; whether its action be slow and regular, or rapid and tumultuous as sometimes occurs, vagus stimulation continues effective and causes an immediate standstill. This fact affords a convenient means of demonstrating the 'quelling' action of the vagus upon the movements of the heart.

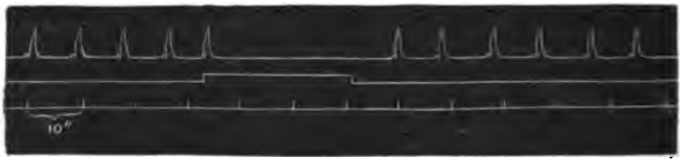


FIG. 50.

Arrest of heart by excitation of vagus 20 minutes after decapitation.

Arrest of the heart may be also brought about by a reflex action of the vagus; mechanical stimulation of the intestine of the frog, or of the tail of the eel, stimulation of the central end of most afferent nerves, including the vagus itself, will cause this reflex inhibition; it is not produced after section of the vagi, nor after destruction of the spinal bulb, thus proving that the vagi are really the efferent channels of the arrest produced by peripheral stimulation. *Fainting* is in many cases due to a temporary arrest of the heart by reflex inhibition. The variations in the heart's frequency which accompany respiratory variations of blood-pressure disappear after section of the vagi;

the *expiratory diminution* of frequency (*vide* p. 140) is therefore due to vagus action, and is probably a reflex caused by some form of pulmonary stimulation. The act of *swallowing* temporarily interferes with the constant inhibitory action of the vagus; sipping a glass of water may thus cause the heart's frequency to rise twenty or thirty beats per minute.

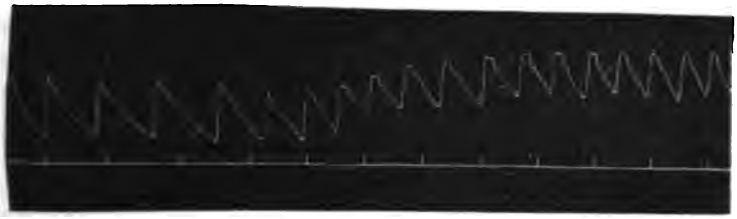


FIG. 51.—MAN.

Effect of sipping water upon pulse-frequency; the heart beats faster owing to diminished vagus control, and the blood-pressure is raised.

The Trophic Theory.—A theory at present current on the authority of Gaskell, attributes the inhibitory effects of the vagus to its 'trophic' or 'anabolic' action on the heart muscle. The facts which laid the foundation of this theory were the augmentor or 'beneficial' effects on the frog's heart produced by stimulation of the vago-sympathetic trunk, which were at the time attributed to vagus action. Gaskell considers that whereas ordinary motor nerves produce action as a consequence of their katabolic effect, inhibitory nerves, *e.g.* the vagus, produce arrest of action as a consequence of their anabolic effect. He regards the negative variation of ordinary excited muscle as the sign of a katabolic effect, and finds that arrested cardiac muscle gives a positive variation on vagus stimulation which he regards as the sign of an anabolic effect. His experiment in demonstration of a positive variation was performed on the auricle of the tortoise heart, prepared in a special manner, no analogous effects being discoverable on the inhibited hearts of other animals.

Accelerator nerves.—The converse of inhibition, as regards the heart, is acceleration; accelerator influences are conveyed from the spinal cord to the heart by the channel of branches of the sympathetic which form part of the cardiac nerves and plexus, their exact anatomy differing in different animals. *Section* of these nerves is without any constant result as regards the heart's beat; they are not continuously but only *occasionally* conveying accelerator influence, unlike the vagus which is *continuously* conveying inhibitory influence. On the other hand, the *excitation* of the peripheral ends of divided accelerators ha a uniform and well-marked effect—the frequency of the heart' beat is increased. Compared with the vagus effects as regard latency and duration, the accelerans effect is slowly produce and slowly develops to its maximum. The inhibitory and accelerator nerves are not regarded as true antagonists; if bot be simultaneously excited to action, the effects do not balanc and neutralise each other, but arrest during stimulation, an acceleration after stimulation are the usual consequences. It i by these channels that accelerator influences reach the hear when the spinal cord is directly stimulated.

Vaso-motor nerves.—The arteries are not inert pipes, bu essentially muscular tubes which are played upon and excited t contract or to dilate by vaso-motor nerves; nerves, the excitatio of which causes contraction of the arterial muscle, are calle *vaso-constrictors*; nerves, the excitation of which causes dilata tion, are called *vaso-dilatators*. It is easy to understand th action of a constricting nerve, it is difficult to understand tha of a dilating nerve; it is certain, however, that vaso-dilatatio does take place as an active, positive, and immediate chang and not merely as a negative and passive change, or, as a after-effect, a mere diminution of previous vaso-constrictio The action of a dilating nerve is closely analogous with that the cardiac inhibitory nerve—the vagus. Each interferes wit and suspends the action of muscle—of cardiac muscle in th one case, or of arterial muscle in the other. Vaso-constricto are widely distributed throughout the body; their existence wa first discovered in the cervical sympathetic, and has since bee demonstrated in the splanchnic nerves and in the nerves of th extremities. Vaso-dilatators are also widely distributed throug out the body, though in consequence of the preponderatin influence of vaso-constrictor fibres their action is in many cas masked. Their existence was first discovered on the chor tympani, as regards its action upon the vessels of the submaxi lary gland; they have since been demonstrated in the ner erigentes, in several branches of the trigeminal, in the nerves the extremities, in the purely muscular nerves, and even in t cervical sympathetic itself.

the long series of experiments alluded to above, tv in particular are fundamental to the subject of vaso-motor action; these are (1) the experiment of the cervical sympathetic on the rabbit, (2) the experiment of the chorda tympani on the dog.

Cervical sympathetic of rabbit.—If the cervical sympathetic of one side be exposed and *divided*, the vessels of the corresponding side of the head become dilated and the temperature of the parts is increased. The division of the nerve has interrupted constant vaso-constrictor influence passing upwards in the cervical sympathetic. If now the cephalic end of the nerve be *excited*, the previously dilated vessels contract and the temperature of the parts is diminished. This double experiment, the results of which are clear and uniform, marks out the cervical sympathetic as the type and representative of vaso-constrictor nerves, which, as we shall learn from other experiments, are widely distributed throughout the body.

Chorda tympani of dog.—Section of the chorda tympani does not produce any definite or constant effects upon the circulation of the submaxillary gland. Excitation of the peripheral end of the nerve causes an immediate and striking change. The previously pale gland becomes vividly red, and whereas previous to excitation of the nerve black venous blood dribbled out of a divided vein, the blood is now bright scarlet and escapes in jets. All these changes prove that the small arteries of the gland have become dilated, so that the arterial blood passes rapidly and with little change through the capillaries, and the arterial pulse is propagated through them into the veins, giving a venous pulse.

Experiments upon the *nerves of the limbs*—more particularly upon the sciatic—have been numerous and their results conflicting. Diametrically opposite assertions have been made—that the sciatic contains only constricting fibres—that it contains only dilating fibres—that it contains both kinds of fibres. The last assertion is probably correct, and the conflicting data are presumably due to differences in the methods and in the circumstances of experiment. The usual effect of section of the sciatic nerve is vaso-dilatation, which however gradually subsides, the paralysed vessels recovering their original 'tone' in the course of a few days or weeks; the usual *immediate* effect of excitation of the peripheral end of the divided nerve is a brief vaso-constriction, which however soon gives way to vaso-dilatation. As regards methods of observation the following tests have been employed:—temperature observations, manometer observations, changes in colour and changes of a bleeding surface; vaso-constriction is indicated by a fall of temperature, by pallor of the skin, by a fall of venous pressure or by less copious bleeding from a wound; vaso-dilatation by a rise of temperature by flushing of the skin, by a rise of venous pressure or by mor copious bleeding from a wound. The temperature test gives les immediate information than the others; the thermometer is comparatively sluggish instrument reacting slowly to changes o temperature, moreover changes of temperature are not instantl produced by changes of the circulation, so that it might easil happen that brief changes of the circulation should escape notic by this method. And indeed it is to be remarked that the ther mometer has been the instrument most relied on by thos observers who have denied the existence of vaso-constrictors i the sciatic nerve. As regards the circumstances of experimen those most influencing the results are the state of the nerve, th surrounding temperature, and the frequency of stimulatio Excitation of a fatigued nerve, or of a nerve which in cons quence of previous section has begun to degenerate, is more a to give signs of vaso-dilatation, while excitation of a fresh ner usually gives signs of vaso-constriction; it appears as if vas constrictor were less resistant than vaso-dilatator fibres, t former being the first to give way when the nerve is fatigued degenerating. If the surrounding temperature is high, excit tion of the nerve is more apt to cause vaso-constriction than the surrounding temperature is low, when vaso-dilatation more likely to be produced; it appears as if in each case t state of the vessels became reversed by the nerve excitation; the warm medium they are dilated and excitation constri them, in the cold they are contracted and excitation dila them. Rapidly repeated stimuli are more suitable to t demonstration of vaso-constriction, a succession of single stim at longer intervals (1 to 2 sec.) to that of vaso-dilatation.

The *splanchnic nerves* govern a very large vascular district that of the digestive viscera. The effects of their division and their excitation are of corresponding magnitude, and such as cause great variations of the general blood-pressure. Phys logically they are vaso-constrictors, as is unmistakably sho by section and excitation of their peripheral cut ends. Secti causes paralysis of the intestinal vessels, which dilate and acco modate a large quantity of blood; this is derived from the remainder of the system, and the general blood-pressure consequently falls—to $\frac{1}{2}$ or it may be to $\frac{1}{3}$ of its original height—to such a degree in fact that death is imminent or actually occurs owing to the deficient circulation. Excitation of the cut nerves temporarily restores the blood-pressure to or above its original height, in consequence of constriction of the mesenteric and portal vessels. These efferent nerves are in intimate functional relation with an afferent nerve, the depressor nerve, the excitation of which causes reflex inhibition of splanchnic vaso-constriction.

The nervi erigentes arise from the second and third sacral nerves, and, passing through the hypogastric plexus, are distributed to the penis, bladder, and rectum. Section of these nerves causes no obvious change, but excitation of the peripheral end causes erection of the penis attributable to vascular dilatation (Eckhardt). Excitation of the N. pudendus has an opposite effect, from which we must conclude that it contains vaso-constrictor fibres (Lovèn).

The dog's mouth.—In consequence of the striking results on the rabbit's ear of excitation of the cervical sympathetic, we are led to consider this nerve as the typical example of vaso-constrictor nerves. The more recent and no less striking experiment by Dastre and Morat on the dog shows that the cervical sympathetic may also contain dilating fibres. Excitation of the upper end of the divided nerve causes the corresponding half of the mouth (tongue, lips, cheeks, and gum) to flush immediately and vividly. The existence of *pulmonary vaso-motor* nerves has been positively affirmed and as positively denied; they probably do not exist, or, if they exist, their action is quite insignificant.

Central Control.—The regulation of the vascular system is administered by the central nervous system, viz. the medulla oblongata or spinal bulb, and the spinal cord, from which the vascular and cardiac nerves take origin, the particular parts from which they spring being spoken of as their 'centres'[1] and comprising (1) the vagus centre in the bulb, (2) the accelerator centre in the cord, (3) the principal vaso-motor centre in the bulb, (4) action is more affected by chloral than dilating action. These results refer to the reflex effects of stimulation of afferent nerves ; very similar results are obtained by the direct stimulation o efferent (vaso-motor) nerves. The sciatic, for instance, if it peripheral end be stimulated, gives, if fresh, vaso-constriction— but if fatigued, vaso-dilatation. Here again it appears tha dilating outlasts constricting action. The effects are such as t remind us of those obtained by prolonged stimulation of th cardiac nerves; when vagus and accelerans are simultaneousl excited, the vagus effect wears away comparatively quickly, an the accelerator effect is left unmasked.

---

[1] Anatomically a centre is a nucleus or ganglion of grey matter from which nerves originate; histologically this grey matter is composed of nerve-cells with which nerve-fibres are connected. Physiologically a centre is a mediator between centripetal and centrifugal nerve impulses; it receives centripetal impulses from afferent nerves, and emits centrifugal impulses by efferent nerves. 'Spinal bulb' and 'medulla oblongata' are used indifferently as synonymous terms.

Local vaso-motor reflexes.—As has been stated, the effect o the stimulation of afferent nerves is usually vaso-constrictio and rise of general blood-pressure, but sometimes the revers The local effects are precisely opposite; usually the circulatio becomes more active in a part of which an afferent nerve i excited, the vessels of the part dilate, while the rise of th general blood-pressure shows that other vascular districts of th body at the same time contract; both factors thus concur i promoting the more copious blood-supply of the district, a afferent nerve of which is stimulated; the effect is produced b experimental stimulation of the central end of a divided ner containing afferent fibres, or by irritation of the cutaneo periphery, the nerves of which are intact, or by excited action a part. Irritation of the central end of the great auricul nerve (in the rabbit) and consequent dilatation of the vessels the ear, irritation of the central end of the tibial nerve a consequent dilatation of the external saphena vein, are the t best known instances of reflex vaso-dilatation by experiment stimuli; the effect of a blister is a familiar instance of refl vaso-dilatation by cutaneous stimulation; the more active circ lation in contracting than in resting muscle, in secreting th in resting gland, are physiological instances of reflex vaso-dila tion in consequence of increased activity of a part, to which m be added as a pathological instance the increased activity of t circulation in an ' inflamed ' part. In all these cases periphe activity causes centripetal stimulation, the reflex effects of wh are vaso-dilatation and increased blood-supply.

An experiment of Brown-Séquard and Tholozan may quoted in evidence of the possibility of *crossed reflex vaso-c striction*; these observers detected a fall of temperature of left hand when the right hand was plunged in cold water, and *vice versâ.*

The Lymphatic Circulation.—The lymph moves in a circle, but very slowly in comparison with the blood circulation; it exudes into the tissue-spaces through the walls of the capillaries, and is carried back to the blood by lymphatic capillaries and vessels, converging from all parts to form the thoracic ducts, which discharge their contents into the subclavian veins. The forces by which the current of lymph is kept up are, the exudation pressure under which lymph is discharged from the blood, and the accidental compression of lymphatic spaces and vessels by muscular movements, and by the arterial pulse throughout the body; the lymphatic vessels are abundantly beset with valves which permit fluid to pass towards the heart, but prevent it from being driven backwards towards the tissues; moreover, the walls of the larger vessels are contractile; a slight favouring action is attributed to the current of blood in the subclavian veins, and the aspiratory action of inspiration must act in the same sense; in the lacteals, in which valves are abundant, the flow of chyle is promoted by the pumping action of the villi and by any movement of the intestine.

In some of the lower animals, special contractile organs, the so-called lymph-hearts, by their rhythmic action, forward the movement of the lymph. The frog possesses two such pairs of hearts, an anterior pair beneath the scapula, and a posterior pair in the ileo-coccygeal space; their functional relations are in many respects analogous with those of the blood-heart; their nervous supply is derived from the second and from the tenth pairs of spinal nerves, and from the sympathetic; the muscle which enters into their composition is similar to that of the heart; and although the experimental effects of nerve-section and nerve-stimulation are not so precise as might be desired, we have evidence that the action of the lymph-hearts, while locally independent of the spinal cord, is subject to reflex inhibition like that of the heart itself. The rate of beat, usually ranging from 60 to 80 per minute, is however far more variable, and each lymph-heart has its own rhythm independent of that of the others.

Observations on the pressure and flow of fluid in the larger lymph-vessels indicate a far more sluggish circulation than in the case of the blood; in the thoracic duct the pressure is between 1 and 2 cm. of water, and the current flows at a rate below $\frac{1}{2}$ cm. per second. In its passage through the lymph-glands, the fluid receives newly formed leucocytes, and becomes more highly charged with proteid. The glands just alluded to are essentially masses of lymphoid tissue, bordering upon what is termed the lymph-channel, through which the fluid percolates from afferent to efferent lymphatics of the glands. This lymphoid tissue is the source of leucocytes, and plays the part of a physiological filter in relation to lymphatic absorption; this is illustrated by the effects of poisoned wounds such as are frequently received in dissecting or *post-mortem* work; inflammation set up by septic matter extends along the lymphatics to the lymphatic glands, where it usually remains localised.

The total amount of lymph in the body is estimated at 25 to 30 per cent. of the body-weight, *i.e.* no less than three or four times the amount of blood, but the data upon which the estimate is formed are very imperfect, and the estimate is quoted merely to signify that the amount is very large.

An excessive exudation of lymph, not carried back by the lymphatics to the venous system, is known as œdema or dropsy; the accumulation may be general or local, it may occur in the connective tissue or in serous cavities, where it forms the lymphatic effusions already alluded to—hydrocele, pleuritic, and pericardiac fluids.

CHAPTER IV

RESPIRATION

PAGE

115 Internal and external respiration—Stages of the process of respiration—Historical sketch—Present state of our knowledge.

117 Physiological anatomy of the lungs and thorax—Perforation of the thorax and collapse of the lungs—Pneumothorax—Pleurisy—Pleuritic effusion—Extent of pulmonary surface.

119 Inspiration and expiration; inspiratory and expiratory muscles—Types of respiratory movements, thoracic and abdominal.

120 Tidal air—Complemental air—Supplemental air—Residual air—Vital capacity—Capacity of equilibrium.

121 Composition of expired as compared with atmospheric air—The respiratory quotient—Organic emanations—Amount of fresh air necessary; ventilation.

124 Frequency and rhythm of respiratory movements; Apnœa, Dyspnœa, and Asphyxia—Cheyne-Stokes breathing.

128 **Variations of respiratory activity under different conditions:** Cold-blooded and warm-blooded animals—Temperature—Age—Exercise—Food—Variations of the respiratory quotient.

131 **Respiration of muscle:** Methods—Muscle in air—in nitrogen—in vacuo. Artificial circulation—Tetanus—Rigor.

135 **Partial pressure of O_2 and of CO_2:** In atmospheric air—In alveolar air—In arterial blood—In venous blood—In lymph or tissue—Intrapulmonary and intrathoracic pressure.

140 **Influence of respiration upon circulation:** By movements of the chest—By nerves—By quality of blood—Obstructed respiration—Müller's experiment—Valsalva's experiment—Compressed air—Rarefied air—Artificial respiration.

145 **Control of respiration by the Nervous System:** Normal respiration is automatic, but can be altered by voluntary and reflex stimuli—The respiratory centre: State of the blood—Afferent nerves: The vagus—The superior laryngeal—The fifth nerve.

THE LARYNX

148 Cartilages—Ligaments—Muscles—Nerves—The vocal cords—Their movements with respiration and with vocalisation—Inferior laryngeal nerve—Effects of section and of excitation—Superior laryngeal nerve.

IN common language, the term respiration is used indifferently for the visible act of breathing, and for the invisible gaseous exchanges taking place between the air and a living body. We have at the outset to distinguish in the complete process of respiration, two stages: *external* respiration, or the mechanism of aeration; and *internal* respiration, or the actual exchange of gases which takes place in the tissues of the body. The essential function which is the property of every living cell, vegetable and animal, of low as of high degree, is internal respiration; external respiration is accessory to it inasmuch as it is the preliminary mechanism, varying in various cases, by which that essential function is made possible. Thus in the lowest organisms we have the whole process effected by direct diffusion without the intermediation of respiratory or circulatory organs; among higher animals (vertebrata) we have a series of preliminary phenomena effected through a respiratory organ—gills or skin or lungs—and through a circulating medium, the blood; by these means oxygen is carried to every living cell of the body, and carbon dioxide is carried away. Strictly speaking, the process is divisible into four stages: (1), the mechanism of breathing, viz. the respiratory movements; (2), pulmonary or external respiration, viz. the exchange of gases taking place between the air and the pulmonary blood; (3), systemic or internal respiration, viz. the exchange of gases taking place between arterial blood and lymph or tissue; (4) the chemical changes which take place in living aerated tissue. That these are the links into which the respiration of a mammalian animal is naturally divisible, will be clearly brought out by a brief historical sketch of the stages through which our knowledge of the subject has progressed.

I. Black, in 1757, showed that the end-product of respiration is identical with that of combustion, viz. carbon dioxide; Priestley, in 1775, discovered oxygen, compared respiration with combustion, and contrasted the respiration of plants with that of animals. Lavoisier established the fundamental facts definitely, viz. that respiration, like combustion, consists in consumption of oxygen with production of carbon dioxide, and evolution of heat.

II. Lavoisier's followers believed that the production of carbon dioxide was the immediate consequence of the consumption of oxygen, and taught that respiration was a direct oxidation or union of oxygen with carbon taking place in the lungs.

III. That this is not the case was proved by the extraction of the blood-gases by Magnus in 1837. The fact that oxygen and carbon dioxide exist as such in the blood, proves that the lung at any rate is not the seat of oxidation.

IV. Nor is it the blood (as was for a time supposed), for carbon dioxide was extracted by Pflüger and his pupils from the lymph and from muscular tissue.

V. Thus far the process is traced back to its source in the living tissues; but now, finally, it has been shown in the laboratories of Pflüger, of Ludwig, and of Hermann, that the process itself is no direct union of oxygen with carbon, but that oxygen is first integrated in some complex body, by the subsequent disintegration of which carbon dioxide is produced. That carbon dioxide is not the *immediate* consequence of oxygen supply is demonstrated by the fact that living tissue, or even an entire animal, such as a frog, goes on exhaling carbon dioxide in an atmosphere free of oxygen.

Thus the links in the chain of respiration, as we now know them, are as follows:—Oxygen, introduced into the lung by muscular movement, diffuses into the pulmonary blood and is conveyed to the systemic capillaries, whence it diffuses into the lymph and tissues; here it enters and forms part of some complex compound which subsequently yields carbon dioxide as a disintegration product; carbon dioxide diffuses from the lymph to the blood, is therein carried to the lung, whence it diffuses into the air.

The mechanism of pulmonary or external respiration includes (1) the mechanical movements of the chest and lungs, and (2) the process of gaseous diffusion between the air in the lungs and the gases in the blood.

Physiological anatomy of the lungs and thorax.—The thorax and lungs together constitute a bellows, by the alternate enlargement and shrinkage of which air is drawn in and driven out through the nostrils, windpipe, and air-passages. The lungs are practically a many-chambered bag contained in the thorax, not attached to its walls, but in close apposition to them; the outer surface of the lungs and the inner surface of the thorax are covered by a serous membrane, the *pleura*; between these two layers is the pleural cavity, which in health is practically empty. Lungs and thorax move conjointly, expansion and contraction of the thorax entailing expansion and contraction of the lungs; when the thorax and lungs expand, air enters the lungs by atmospheric pressure; when the thorax contracts, air is driven out into the atmosphere.

The thorax is a closed cavity; if it should be broken into by accident or by operation, the lung does not remain in apposition with the chest-wall, but shrinks away from it and collapses, while the chest-wall, relieved of the elastic traction normally exercised by the lung, undergoes a slight expansion. The pleural cavity is normally non-existent as an actual space; the pulmonary and thoracic layers of the pleura are in close apposition, moistened by a barely appreciable amount of lymph. If, however, the thorax should be perforated, the lung in collapsing separates the two layers of the pleura, and the pleural cavity is occupied by air (pneumothorax). If the membrane should become inflamed, lymph and leucocytes are effused into the pleural cavity (pleuritic effusion), and as one of the after effects of inflammation it may happen that 'adhesions' are formed between the two layers of the pleura, leading to a more or less complete obliteration of the pleural cavity. Collapse of both lungs causes immediate death, collapse of only one lung is dangerous, but not necessarily fatal. During fœtal life the lung contains no air and exercises no elasticity (atelectasis); after birth, with the establishment of pulmonary respiration, the alveoli are opened out, and by the subsequent growth of the thorax the lungs undergo a further passive expansion.

The lung ultimately consists of an aggregation of minute chambers—the *alveoli* or *air-cells*—the walls of which are covered with a close network of capillaries. This subdivision of the air-sac affords a very extensive surface exposed to the air which penetrates to the alveoli; and the capillary network affords a similar spreading out of the blood into what amounts to a thin sheet of very great area. It has been estimated that the alveolar surface amounts to no less than 200 square meters, and that the total capillary surface is equal to 150 square meters; the thickness of the capillary sheet of blood may be reckoned as being somewhat greater than that of a single blood-corpuscle, say 10 μ. From these data it may be realised how favourable are the conditions to the prompt aeration of the blood by the lung. At any moment it contains in its capillaries nearly 1,500 c.c. of blood spread out in a thin sheet 150 square meters in area, and only $\frac{1}{100}$ millimeter in thickness. This extensive film of blood is separated from the alveolar air by the endothelium, which lines the pulmonary capillaries and by that which lines the inner surface of the alveoli. Through this septum the exchange of gases between air and blood is effectually and rapidly carried out.

Each act of respiration is composed of two phases—*inspiration* by expansion of the thorax and lungs, *expiration* by their shrinkage. Normally, inspiration is effected by muscular action, while expiration is literally a 'shrinkage' to the original volume by virtue of the elasticity of the lungs. It is only when respiration is forced or laboured that expiration is assisted by the action of thoracic muscles. The muscles acting in *normal inspiration* are the diaphragm and external intercostals with the scaleni, the inter-cartilaginous portion of the internal intercostals, the levatores costarum, and the quadratus lumborum. In *laboured inspiration* other muscles come into action—the serrati (magnus, superior, and inferior), the sterno-mastoid, and, indeed, any muscle extending between the thorax and upper extremities, *e.g.* pectorales (major and minor), latissimus dorsi. These last-named muscles, which ordinarily act from the thorax as a fixed point of origin, now act upon the thorax, fixed objects being grasped with the hands so that the humerus and scapula afford points of origin instead of points of insertion. At the same time the vertebral column is fixed and extended by the dorsal muscles. In *normal expiration*, as already stated, the chief factor is the elastic recoil of the lung to its position of rest, with perhaps some slight assistance by the interosseous portions of the internal intercostals and by the triangularis sterni. In *laboured expiration* the abdominal muscles assist by fixing and compressing the abdomen, forcing the diaphragm upwards, and constricting the lower part of the thorax.

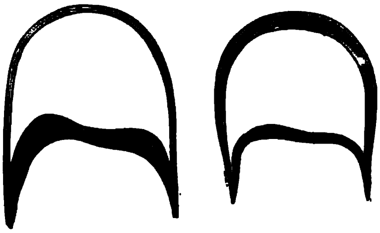


FIG. 53.

To illustrate the 'diaphragmatic' and 'costal' types in the male and in the female. The shaded spaces are intended to indicate the range of movement (much exaggerated) of the diaphragm, and of the chest in the two cases.

The most important of the muscles above enumerated are those which always act in respiration, *i.e.* those of normal inspiration, viz. the diaphragm and the external intercostals (in conjunction with the scaleni). The diaphragm is a dome-shaped sheet of muscle forming the partition between thorax and abdomen. The external intercostals form two lateral sheets of muscle composed of a series of slips extending from rib to rib. The scaleni fix the first two ribs, thus affording an essential condition of effective action as regards elevation of the ribs by the series of external intercostals; each of these muscles acts from the rib above as its relatively fixed point upon the rib below as a relatively movable lever which it elevates; the quadratus lumborum, acting from the pelvis upon the last rib, affords a fixed point to the contracting diaphragm. By these means the thorax is enlarged in all its diameters, (1) vertically by the descent of the diaphragm, (2) laterally by the elevation of the ribs, and (3) in an antero-posterior diameter by the elevation of the ribs and of the sternum. And according as one or other of these muscular agencies take chief part in such inspiratory movement, two types of respiration are distinguished—the costal or thoracic, and the diaphragmatic or abdominal. In the thoracic type, which is characteristic of women, the thoracic muscles play the greater part; in the abdominal type, which is characteristic of men, the diaphragm is comparatively more effectual. But it is a mistake to suppose that these are fundamental sexual differences; they are probably due to differences of dress.

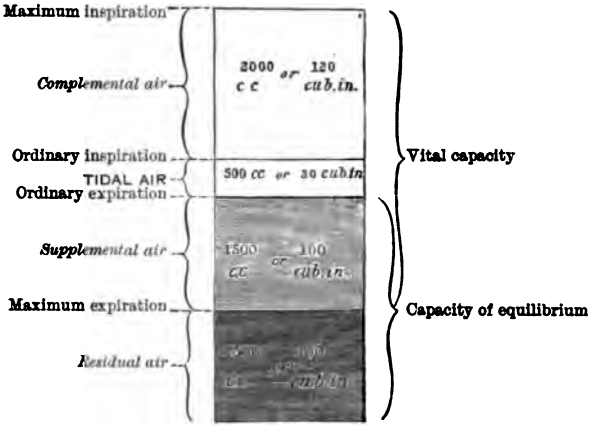


FIG. 54.

Amounts of air contained by the lungs in various phases of ordinary and of forced respiration.

In ordinary easy breathing, a moderate amount of air is taken into the chest with each inspiration, and given out with the succeeding expiration. This air is called the *tidal* air, and amounts to about ½ litre, or 500 c.c., or 30 cubic inches. Beyond this ordinary or tidal amount it is possible by an extraordinary effort of inspiration to introduce into the chest a further 1,500 to 2,000 c.c. of air, which amount is termed *complemental* air, or by an extraordinary effort of expiration to expel 1,500 c.c. (in excess of the normal tide) which is termed the *supplemental* air. After the most complete possible expiration, there is left in the lungs a quantity of air amounting to another 1,500 c.c., which no effort can expel; this is the *residual* air. In relation to this matter, two other terms require to be defined—the *vital capacity*, amounting to between 3,000 and 4,000 c.c., is used to denote the amount of air which can be given out by the deepest possible expiration after the deepest possible inspiration; the *capacity of equilibrium* or *stationary air*, amounting to about 3,000 c.c., is the cubic capacity of the chest after normal expiration. These terms will be best brought to mind by referring to the diagram (fig. 54).

We have seen that at each respiration the lungs are not entirely emptied of and refilled with air, but that the greater proportion of their contents remains stationary, while a small proportion only, nearest to the outlet (nose and mouth), is actually exchanged. It is by the rapid diffusion of gases taking place between the stationary and the fresh tidal air, that the former discharges carbon dioxide and is replenished with oxygen. We have now to consider in detail the manner in which the pulmonary blood and air influence each other. The effect of the blood upon the air is known by comparing expired with atmospheric air; the effect of air upon blood by comparing pulmonary venous with pulmonary arterial blood.

Expired air as compared with atmospheric air contains about 5 per cent. less oxygen and 4 per cent. more CO_2. It is warmer, saturated with moisture, fouled by organic emanations, and slightly diminished in volume.

The differences between pulmonary venous and pulmonary arterial blood must obviously correspond with these—theoretically at least—seeing that any gained or lost matter in expired air must, regarded from the other side, be lost or gained matter from the pulmonary venous blood. Practically, however, we can only say that the difference between blood in the pulmonary artery and in the pulmonary veins is that the former is blacker, contains more carbon dioxide and less oxygen than the latter; in a word, that the former is 'venous' in character, the latter 'arterial.' We cannot state, as directly demonstrated, the minute differences which must exist either in temperature or in amount of water, or in amount of organic matter. To return to the differences between expired and atmospheric air, it is to be observed that the minus quantity of oxygen is greater than the plus quantity of carbon dioxide; with this inequality corresponds the fact that the volume of expired air is slightly less than that of the previously inspired air. The fraction denoting the ratio $\frac{\text{Vol } CO_2 \text{ exhaled}}{\text{Vol } O_2 \text{ absorbed}}$ is spoken of as the *respiratory quotient*; normally this fraction is about $\frac{4}{5}$ or ·8.

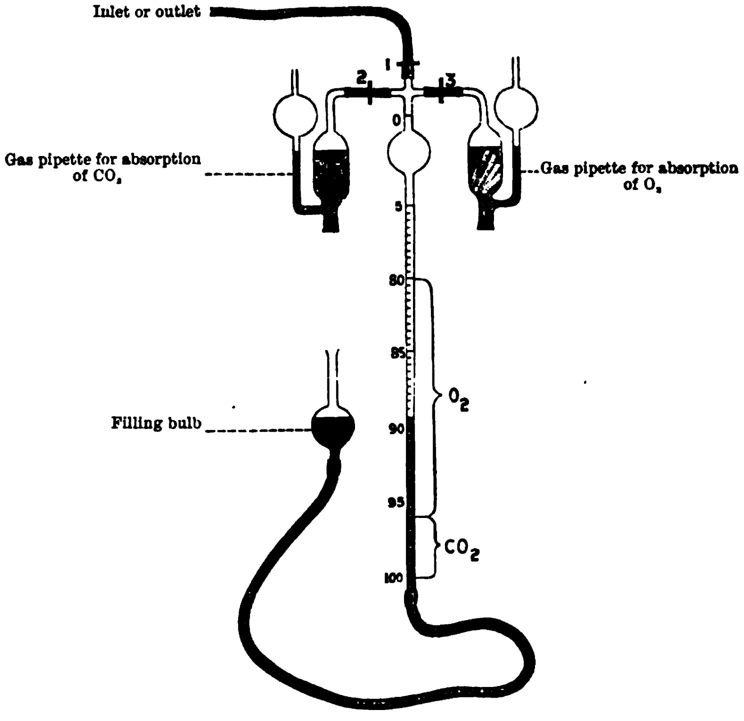

Inlet or outlet
1
2
3
0
Gas pipette for absorption of CO_2
Gas pipette for absorption of O_2
5
80
85
O_2
Filling bulb
90
95
CO_2
100

FIG. 55.—ESTIMATION OF O_2 AND OF CO_2 IN EXPIRED AIR.

A 100 c.c. measuring tube graduated in tenths of a c.c. between 75 and 100. A filling bulb. Two gas pipettes. The measuring tube communicates by three tubes guarded by simple taps 1, 2, 3, with the inlet and with the gas pipettes. It is first charged with acidulated water up to the zero mark by raising the filling bulb, tap 1 being open, it is then filled with 100 c.c. of expired air, the filling bulb being lowered until the fluid in the burette has fallen to the 100 mark. Tap 1 is now closed, the measuring tube containing 100 c.c. of expired air with unknown quantities of CO_2 and of O_2. The amount of CO_2 is ascertained as follows: Tap 2 being opened, the air is expelled into a gas pipette containing KHO by raising the filling bulb until the fluid has risen to the zero mark of the measuring tube. Tap 2 is now closed, and the air left in the gas pipette for about a minute, during which the CO_2 present is entirely absorbed. The air is then drawn back into the measuring tube by lowering the filling bulb while tap 2 is open. The volume of air (minus the CO_2, which is being absorbed) is read, the filling bulb being adjusted so that its contents are at the same level as the fluid in the burette. The amount of O_2 is next ascertained in a precisely similar manner by sending the air into a second gas pipette containing sticks of phosphorus in water, and measuring the loss of volume (due to absorption of O_2) in the air when drawn back into the tube. A gas pipette works thus: fluid in its lower half is displaced into its upper half, when air is driven in from the measuring tube, and returns to its original place, when air is drawn back. If desired, the apparatus can be connected with a vessel in which a frog or mouse or excised muscle has been placed and the consequent alterations of the gases O_2 and CO_2 measured in a similar manner.

The analysis of a single sample of expired air is not a reliable indication of respiratory activity. It is necessary to know the total amount of air expired in a given time and to analyse a mixed sample of that total amount corrected to standard temperature and pressure. These conditions are fulfilled by Zuntz' complete apparatus. A gasometer records the total amount of air expired and at the same time unwinds a filling apparatus so as to collect in a measuring tube an average sample of the total air expired. If, for instance, during 5 minutes, 40 litres of air were expired, and if an average sample of 100 c.c. collected during that period contained 4 c.c. more CO_2 and 4·5 c.c. less oxygen than atmospheric air, the average per minute would be 320 c.c. CO_2 discharged, 360 c.c. O_2 absorbed, and the respiratory quotient = $\frac{8}{9}$ or ·88.

To examine the respiratory exchange of animals it is necessary to connect the gasometer with a tube tied into the trachea, or with an air-tight 'respiration chamber' in which the animal or man is confined; in this case, air is drawn through the chamber and gasometer by an aspirator. The older apparatus of Pettenkofer and Voit, as well as that of Regnault and Reiset, was constructed upon this last principle, including (1) a respiration chamber, (2) a gasometer, (3) an aspirator, and (4) a series of baryta tubes in which excreted CO_2 was absorbed and weighed, the oxygen item being undetermined. For experiments extending over long periods, the total amount of CO_2 excreted by a large animal is inconveniently large; the difficulty is met by taking only a measured fraction of the total expired air through the absorption tubes to be weighed.

If for every five volumes of oxygen absorbed, only four volumes of CO_2 are exhaled, one volume of oxygen remains unaccounted for; it is probable that this excess of oxygen which does not reappear in union with carbon, does so in union with hydrogen as water.

A second point, which is of great practical importance, relates to *organic matter* exhaled from the lungs. It is the chief factor in the fouling of air, but though its effect is thus so pronounced, no direct estimate or measurement of its amount can be made. All we may say concerning its nature is that it is probably proteid in character, condensed respiratory moisture giving a faint xanthoproteic reaction. It may, however, be indirectly estimated by measurement of exhaled CO_2, the amount of which indicates to what degree the air is fouled by the more deleterious but impalpable organic emanations of the breath. A rough but excellent guide to the amount of respiratory impurity is the sense of smell. The air of a room in which respiratory CO_2 does not exceed 2 per 10,000 is 'fresh;' when the respiratory CO_2 is between 2 and 4 per 10,000 the room begins to feel close, between 4 and 6 per 10,000 it is decidedly 'close,' between 8 and 10 the air is 'foul,' and beyond this limit intolerable for any length of time. 2 per 10,000 or 1 per 5,000 is thus the limit of expired CO_2 admissible in perfect ventilation, and should never be exceeded.

From these data we may at once calculate the *amount of fresh air* which should circulate through a properly ventilated room, remembering that every 1 c.c. of expired CO_2 is to be diluted by at least 5,000 c.c. of fresh air. An adult expiring 15 times per minute 500 c.c. of air containing 20 c.c. of CO_2, exhales in one hour 18 litres of CO_2, which, to be diluted 5,000 times, requires 90,000 litres of air, *i.e.* the fresh air required during the hour is 90,000 litres, or 3,000 cubic feet. This is the normal amount of fresh air per head per hour, which should be provided for in the ventilation of dwellings intended to be 'healthy.' But although this comparatively high standard of purity is desirable in the air of permanently occupied chambers, we frequently, and without discomfort, remain for short periods in air with a much higher percentage of respiratory CO_2—*e.g.* in theatres or in class-rooms.

Frequency and rhythm of respiratory movements.—We have taken as an average frequency of respiratory movements 15 per minute. The frequency is by no means invariable, anything between 12 and 20 is normal, and the number is subject to many modifying conditions—as age, sex, exercise, health—and also to

FIG. 56.

Tracing of normal respiration of man. The frequency of the act was at the tim 20 per minute; each respiration occupied 3 sec., of which inspiration occupie 1 sec., expiration (inclusive of the expiratory pause) 2 sec. The smaller un undulations (about 4 to each respiration) are caused by the heart-beats.

various emotional and mental states. The frequency of respiration usually bears a definite ratio to pulse frequency, viz. respiration to every 4 or 5 heart-beats. It is greater in th female or child than in the male or adult. It is increased b exercise, and diminished during quiescence. During illnes especially in the febrile state, it is increased. As regards the effects of emotional and mental states we shall more conveniently consider them under the heading 'Influence of the Nervous System.' It need here only be observed that the frequency of respirations should always be noted while the patient is unaware of the proceeding, and not under the influence of any exciting event, because any disturbing cause—the mere fact of turning attention to the act of breathing—may suffice to alter its character and frequency.

An accelerated rate of respiration is accompanied with an increased elimination of CO_2, but this increased elimination is by no means proportional to the greater frequency of respiration; this is accounted for by the fact that each act of respiration is deeper in a slow series than in a rapid series, so that a man breathing 30 times per minute, does not expire anything like twice as much air, nor twice as much carbon dioxide, as a man breathing 15 times per minute. Moreover, the percentage of CO_2 is less in the expired air of shallow than in that of deep respiration.

Dyspnœa. Asphyxia. Apnœa.—Dyspnœa signifies difficult breathing, and is the consequence of any impediment to the free ingress and egress of air from the lungs. If aeration be completely interfered with, as by drowning or by obstruction of the trachea, death by asphyxia is the result. The term asphyxia, which literally signifies pulselessness, is generally taken to cover the entire series of events from the moment when aeration is interfered with, to the cessation of all respiratory and cardiac movements. This series of events as observed upon an animal killed by sudden and complete closure of the trachea is divisible into three stages, (1) that of increasing dyspnœa, culminating in (2) the convulsive stage, which gives way to (3) the period of exhaustion. *During the first stage*, which lasts about a minute, the respiratory movements become stronger and longer, therefore less frequent, the prolongation being chiefly expiratory; the heart beats with increased force and frequency, the blood-pressure rises, the pink or red colour of the tongue or lips darkens and gives place to bluish purple. *During the second stage*, which lasts about a minute, the respiratory movements become violent and convulsive, the convulsions being chiefly expiratory; the heart beats forcibly but less frequently, the blood-pressure keeps high, the dusky colour of the mucous membrane is increased.

That the raised blood-pressure is caused by vaso-constriction rather than by increased heart's force is proved by the fact that the blood-current is at the same time much slower than normal. *During the third stage,* which lasts two or three minutes, movements ebb, the pupils dilate, convulsions cease, respiration becomes less frequent and more shallow, finally ceasing in expiration; the heart beats feebly and unfrequently, or feebly and rapidly, and finally stops, the blood-pressure falls and nearly reaches zero, its decline being frequently marked by Traube-Hering undulations; the dusky mucous membranes become pale and anæmic. *Post mortem* the right side of the heart, the large veins and the lungs are gorged with thick blood, the left side of the heart is empty and contracted.

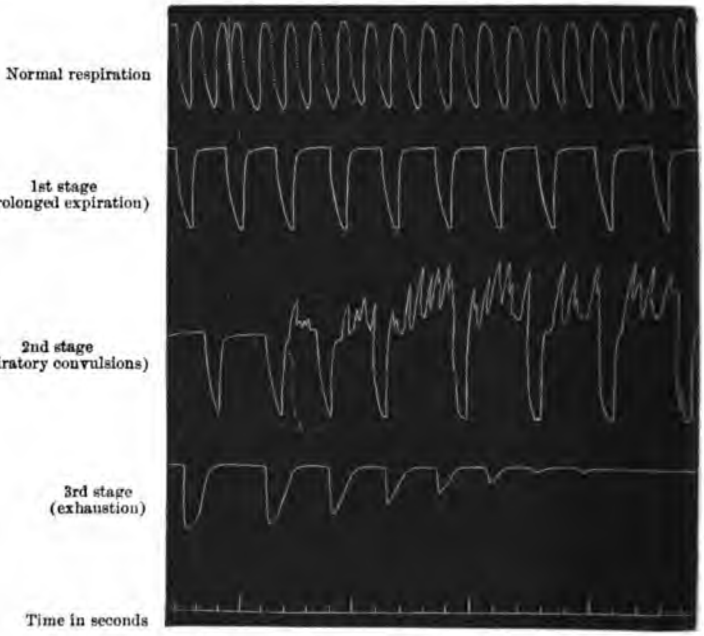


Fig 57.—Asphyxia Tracing. (Rabbit.)
(The line falls with inspiration, rises with expiration.)

Recovery from asphyxia is possible in apparently almost hopeless cases; artificial respiration, *i.e.* rhythmical inflation of the chest by means of bellows, or passive movements of the arms and chest in imitation of inspiration and of expiration, will often cause the heart to resume action, and blood-pressure to be restored; relief of the engorged right auricle by venesection will sometimes set going again a heart which seems to have finally stopped. The practical lesson which these facts enforce is that artificial respiration should be steadily maintained on the bodies of the apparently drowned, and that a jugular vein, especially if visibly distended, may be and should be opened. Artificial respiration is also in common use in the laboratory to keep animals alive when from any cause their spontaneous movements of respiration can no longer be effected.

Apnœa is the opposite of dyspnœa; it is the temporary non-breathing state which is induced by repeated inspiration or by inflation of the lungs. An animal rendered apnœic by artificial respiration remains passive without any effort of respiration for several seconds, and then begins to breathe by very shallow inspirations which gradually deepen. This passive state may be brought about on oneself by repeated deep inspirations, after which it will be found that the breathing may be suspended for a longer period and with greater comfort than in the normal state. The apnœic state has received more than one explanation; it has been referred to a more completely saturated state of arterial blood as regards oxygen, to a provision in the lung itself of a larger and purer air supply, and to an inhibitory effect produced by the mechanical distension of the lungs. Probably all these factors concur to the result, for these reasons :—apnœa in animals is *best* produced by inflation with oxygen, but *can be* produced by inflation with hydrogen or nitrogen; apnœa is *best* produced with the vagi nerves intact, but it *can be* produced after section of both these nerves. Apnœic pauses on man are longer and shorter according as the amount of oxygen inhaled is greater or smaller, but in no constant ratio; the non-correspondence of the two quantities is attributable to the fact that nervous influences are also in play in the maintenance of apnœic pauses; these nervous influences are probably an inhibitory effect transmitted along the vagus to the medulla from the distended lung, and in a minor degree a depression of the excitability of the 'respiratory centre' by blood fully charged with oxygen.

Cheyne-Stokes breathing is characterised by a waxing and waning of the amplitude of the respiratory movements. In a typical and well-marked case, the movements alternately decline to complete cessation and return to an amplitude much above the normal. No definite or conclusive cause can be assigned to this peculiarity of rhythm; it is not—as was once believed to be the case—characteristic of fatty degeneration of the heart, but makes its appearance in a variety of diseases, or in the absence of any disease at all; during normal sleep, particularly in children, a waxing and waning respiratory rhythm is of common occurrence. All we can say in explanation is to point to the fact that the Cheyne-Stokes rhythm is to the respiratory system what the Traube-Hering rhythm is to the vasomotor system; both rhythms are originated by medullary centres and are of about the same frequency, viz. 1 to 3 per minute; indeed the association is sometimes most definite and exact; on the rabbit, for instance, after hæmorrhage, phases of increasing and diminishing amplitude of respiration coincide with rise and fall of arterial blood-pressure; they are instances among many others of the common tendency towards 'pulsatile or rhythmic activity' manifested by all living matter.

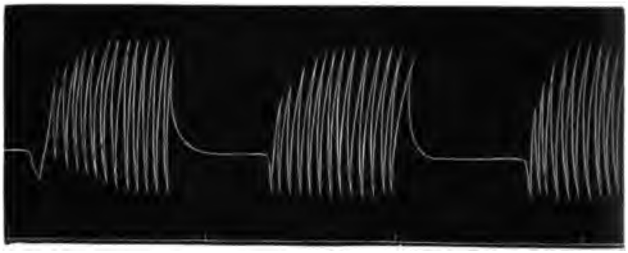


FIG. 58.—CHEYNE-STOKES RESPIRATION.
(Time marked in minutes.)

Variations of respiratory activity under different conditions.—We have learned that the depth and frequency o respiratory movements and consequently the amount of CO excreted vary under different conditions; these variations o the external yield, are the consequence of variations of tissu activity, and therefore afford an index to the variations of th true or internal respiratory activity of the entire body. I should be clearly recognised that the magnitude of the externa respiratory exchange is determined by the degree of interna respiratory activity, and that the converse event—a modification of internal by external respiration—is comparatively sligh or of accidental occurrence. We shall take as our point o departure and standard of reference the average respirator activity of a normal adult. Given, that the average frequenc of respirations is fifteen per minute, that the average amount of tidal air is half a litre or thirty cubic inches, and that expired air contains five volumes per cent. less oxygen and four volumes per cent. more carbon dioxide, a simple calculation gives the average hourly or daily absorption of oxygen and exhalation of carbon dioxide. Their amounts will be as follows:—

	Volume of air expired	CO_2 exhaled		O_2 absorbed	
		by volume	by weight	by volume	by weight
Per respiration . .	500 c.c.	20 c.c.	·039 grm.	25 c.c.	·036 grm.
Per minute (15 r.).	7·5 litres	300 ,,	·591 ,,	375 ,,	·537 ,,
Per hour	450 ,,	18 litres	35·5 ,,	22·5 litres	32·2 ,,
Per day (24 h.) . .	10,800 ,,	432 ,,	852 ,,	540 ,,	773 ,,

Thus a normal adult (weighing 70 kg.) excretes *per diem* 432 litres CO_2 (weighing 852 grammes, and containing 232 grammes of carbon); he absorbs per diem 540 litres O_2 (weighing 773 grammes). Or, otherwise expressed, the average excretion of CO_2 is ¼ litre (weighing ½ gramme) *per kilo per hour*, or about 4 c.c. per kilo per minute.

It should be particularly observed that these are average numbers subject to considerable variation. Thus Pettenkofer and Voit's man, weighing 70 to 73 kilos, yielded daily amounts of CO_2 fluctuating between 695 and 1,038 grammes. Moreover, they are subject to considerable fluctuations in varying conditions of health and of activity; thus an excretion of CO_2 between 3 and 5 c.c. per kilo per minute, *i.e.* 180 and 300 c.c. per kilo per hour, may be regarded as normal.

The subjoined tables contain illustrative numbers from which we may draw certain conclusions.

Animal	Conditions	CO_2 exhaled per kilo per hour
Frog	Temp. 10° to 15°	45 c.c.
,, ...	,, 30° ,, 35°	317 ,,
Hen	—	787 ,,
Hen's egg	during incubation	18 ,,
Marmotte	hibernating	19 ,,
,, ...	awake	667 ,,
Sheep	—	350 ,,
Sheep fœtus	at term weighing 3·5 kg.	30 ,,
Man	—	300 ,,
Rabbit	—	550 ,,
Guinea-pig	—	750 ,,
Horse	at rest	200 ,,
,, ...	at work	1200 ,,

The respiratory activity of cold-blooded is less than that of warm-blooded animals. In cold-blooded animals it varies with temperature, being much greater at a high than at a low temperature; in warm-blooded animals the relation is more complex; so long as their body-temperature remains constant, their respiratory activity diminishes with a rise and increases with a fall of temperature; but if their body temperature is raised or lowered, then the respiratory activity, as measured by CO_2, varies in the same sense, being greater at a high than at a low temperature; with the high temperature of fever the excretion of CO_2 is increased, but the respiratory quotient is not diminished. The variations with age, food, and muscular exercise are particularly instructive. During incubation or pregnancy, and immediately after birth, the respiratory activity is low—new-born animals resist asphyxia for many minutes; during infancy and childhood respiratory activity is greater than during adult life; during adult life it is greater than in old age; the average excretion of CO_2 per kilo per hour is—

In utero	30 c.c.
In childhood	500 „
In adult life	300 „
In old age	250 „

The respiratory activity of different animals under differen conditions is usually estimated by measuring the excretion o CO_2, rather than the absorption of O_2; for observations in whic it is desired to ascertain the respiratory quotient, both measurements must be simultaneously carried out.

Muscular exercise at once raises the excretion of CO_2 above th normal of ordinary life; perfect quietude, on the contrary, lowe it; the excretion of CO_2 by an adult per kilo per hour averages-

During sleep	200 c.c.
„ quietude	250 „
„ ordinary exertion	300 „
„ hard labour	500 „

This relation is confirmed by experiments on animals; th CO_2 excreted by a dog or rabbit with the posterior extremiti paralysed by division of the spinal cord is below normal; th of the same animal when the posterior extremities are tetanis is above normal. Again, the respiratory excretion of CO_2 by curarised animal is diminished, that of a strychninised anim is increased. The diminished production of CO_2, from paralysed as compared with quiescent muscle, will be referred to again when we come to consider the respiration of muscle.

Food increases the production of CO_2, carbohydrates being particularly effective in this direction. The excretion of CO_2 is greater after than before a meal. Light is favourable to respiratory activity; it has been shown by experiments on frogs that the excretion of CO_2 is greater in the light than in darkness, whether the animals have been blinded or not.

Variations in the respiratory quotient, or $\frac{CO_2}{O_2}$ ratio, are of some theoretical importance, but are difficult to determine with accuracy. From the numbers given below it will be seen that the ratio is nearest to unity with carbohydrate diet, and furthest from it in the hibernating condition.

Animal	Condition	Respiratory quotient
Rabbit	Fed on carrots	·9 to 1
"	Fasting	·7
Dog	Flesh diet	·7
"	Bread and fat	·9
"	Fasting	·7
Marmotte	Sleeping	·5
"	Awake	·8
Man	Mixed diet	·8 to ·9

It is also increased by muscular exercise, and diminished during quiescence; the respiratory quotient of a rabbit, for instance, is raised by tetanisation, depressed by curarisation. According to Pettenkofer and Voit the $\frac{CO_2}{O_2}$ ratio is greater during the day than during the night; day-time being favourable to discharge of CO_2, night-time to absorption of O_2.

Respiration of muscle.—Direct data relating to internal respiration are most readily obtained from muscle, and the following plans have been followed:—1. Examination of the gaseous exhalation of muscle enclosed in air, or in an indifferent gas such as nitrogen, or *in vacuo*. 2. Extraction of the gases of muscle itself. 3. Examination of the gaseous exchanges which take place between muscle and the blood by which it is traversed. The last method is specially applicable to warm-blooded animals; in the first two methods the excised muscles of the frog are exclusively employed.

To examine the gaseous exchanges between muscle and air, the posterior extremities of a frog are left suspended in a closed vessel for several hours, at the end of which the air is analysed. It is found to have lost oxygen and gained carbon dioxide. We are not, however, justified in at once attributing the change to a respiratory activity of living muscle, because a control experiment made under similar conditions with dead muscle gives a similar result, the effect in this case being due to putrefaction, which, like respiration, is attended by a consumption of oxygen and a production of carbon dioxide. As regards the consumption of oxygen, it has not been found possible to distinguish a respiratory from a putrefactive effect; moreover, the consumption of oxygen bears no constant relation to the production of carbon dioxide. The oxygen item is, therefore, discarded from further study by this method. But as regards the production of carbon dioxide, it is possible to distinguish a true respiratory from the subsequent putrefactive discharge, and to estimate differences of the respiratory discharge coinciding with differences of muscular activity. Attention is therefore concentrated upon the carbon dioxide item.

Evidence of the above statements is supplied by the comparison of the gaseous exchanges of muscle at rest with those of tetanised muscle, as well as by the gas discharge of muscle in nitrogen or *in vacuo*. There is no demonstrable difference in the amounts of oxygen absorbed by resting and by tetanised muscle, whereas there is a marked difference in the amounts of carbon dioxide exhaled in the two cases. Fresh minced muscle subjected for many hours at a temperature of 20° to 30 to the vacuum of a mercurial pump, yields a continuous discharg of gas; during a first period the discharge is considerable, it the slackens, and again becomes considerable. The first discharg is regarded as respiratory, it consists almost entirely of carbo dioxide; the second discharge is the effect of putrefaction; consists of carbon dioxide and of nitrogen, and it continues f an indefinite period. Muscle suspended *in vacuo* as above, or an indifferent atmosphere of nitrogen, may thus discharge carbo dioxide with no less activity than when it is in an atmosphe containing oxygen. An entire frog washed free of blood by t injection of salt solution, and enclosed in nitrogen or *in vac* continues equally to discharge carbon dioxide. These facts sh conclusively that carbon dioxide is not due to the immedi action of oxygen, but that it is formed in the dissociation some storage compound. The previous action of oxygen has, doubt, contributed to the formation of any such compound; or—as Pflüger expressed it—absorbed oxygen has helped to wind up the clock, discharged carbon dioxide is the sign of its running down. To this storage substance, which, however, is not a real and identified compound but only a hypothetical idea, Hermann has given the name 'Inogen,' (from ἴς, ἰνός, force, or muscle) on account of the supposition that it is the force-producing material in muscular contraction.

The extraction of muscle gas, which is exclusively carbon dioxide, under various conditions of experiment, furnishes data upon which conclusions are based. By raising the temperature to 40° or 50°, muscle is made rigid or 'rigored,' it becomes acid, and the primary discharge of gas is rapidly completed; the addition of phosphoric acid now liberates a further small quantity of carbon dioxide. The carbon dioxide removable by vacuum is termed 'free;' that removable by acid is termed 'fixed;' the total volume of carbon dioxide (free and fixed) thus obtainable from muscle is 1 to 15 vols. per 100. If muscle is suddenly heated to 70°, it is fixed without passing through the stage of true rigor; it is said not to acidify, and no carbon dioxide is discharged; what gas happens to be in the muscle at the time is obtainable from it by vacuum and by acid, but the hypothetical storage-compound 'inogen' is 'fixed' and rendered incapable of further change. This process, technically known as 'scalding,' renders possible certain comparisons. Thus, comparing the amounts of gas obtainable from scalded fresh muscle and from scalded tetanised muscle, much more carbon dioxide is obtainable from the latter than from the former. Comparing scalded fresh muscle with rigored muscle, more carbon dioxide is obtainable from the latter than from the former. Rigored yields more carbon dioxide than tetanised muscle. Finally, by comparing the amounts obtainable (*a*) from fresh rigored muscle, (*b*) from muscle which was first tetanised, then rigored, Hermann found that the rigor gas was less in (*b*) than in (*a*), and that the sum of rigor and of tetanus gases in (*b*) was about equal to the rigor gas obtained from (*a*). The conclusion drawn from these observations is that one and the same substance, 'inogen,' suffers dissociation and yields carbon dioxide in heat-rigor and in muscular contraction.

Fresh muscle minced and boiled for two or three hours yields as much as 100 vols. carbon dioxide per 100 vols. muscle. Muscle which has been tetanised or heat-rigored and allowed to exhale the CO_2 thus produced, subsequently yields about 30 vols. per 100 on boiling. The substance from which carbon dioxide is thus produced is presumably Hermann's inogen, and we are led to suppose that, besides its physiological dissociation in muscular contraction, it dissociates slowly *post mortem* (death-rigor), rapidly at 40° (heat-rigor), is fixed at 70° (scalding), again dissociates at 100° (boiling). In contraction, after death, and at 40°, muscle yields CO_2 and becomes acid; at 70°, although it becomes rigid, it does not yield CO_2 nor become acid; at 100° it yields CO_2 and becomes acid.

The gaseous exchanges taking place between muscle and blood have been more particularly studied by Claude Bernard, by Ludwig, and by Pflüger. Bernard observed the fundamental fact that venous blood coming from muscles is darker during their contraction than during their quiescence. The difference is obviously due to the greater deoxygenating effect of active than of resting muscle, and if we take into account that the amount of blood which passes through the muscles is greater during contraction than during rest in consequence of the vascular dilatation which accompanies contraction, we must recognise that the absolute amount of carbon dioxide produced by muscle is much greater during contraction than during repose. Bernard's estimates do not, however, supply any exact numerical expression for this difference. Ludwig and his pupils, Schmidt and Sczelkow, attempted to fill this gap by the gas-analysis of blood made to circulate artificially through excised muscles, as well as of blood coming from living muscle *in situ*. They confirmed the fundamental fact that active muscle consumes more oxygen and produces more carbon dioxide than resting muscle, but the conditions of experiment were too far removed from the normal for it to be allowable to admit as normal the numerical data obtained. Later experiments in the same laboratory by v. Frey have shown that the consumption of O_2 under such conditions is not more than $\frac{1}{10}$th to $\frac{1}{4}$th the normal, whereas the production of CO_2 and of lactic acid was comparatively large. Pflüger, in conjunction with his pupils, Stintzing and Finkler, criticised and rejected Ludwig's conclusions, in particular the statement that the amount of oxygen in the blood and the amount of the latter passing through the muscle determine the energy of CO_2 production. They uphold by very convincing arguments the precisely opposite doctrine, to wit, that the activity of muscle determines the oxygen consumption, not that the oxygen supply determines muscular activity.

To sum up:—*The activity of muscle-respiration is determined by the activity of muscle, and not vice versâ.*

The consumption of oxygen is determined by the oxygen requirements of tissue, not by the amount of oxygen available.

The exhalation of carbon dioxide is the most reliable indicator of muscle respiration.

By integration of oxygen a force-yielding storage substance is formed.

By disintegration of this substance carbon dioxide is liberated, in company with heat, work, acid, and an alteration of electrical potential.

'Pressure' or 'tension' of gas. 'Partial pressure.'—The pressure of the atmosphere is equivalent to that of a column of mercury about 75 centimetres high.

Atmospheric air is a mechanical mixture of oxygen and nitrogen—in round numbers 1 part oxygen to 4 parts nitrogen.

The pressures of oxygen and of nitrogen in the mixture are proportionate with their respective volumes, *i.e.* $\frac{1}{5}$ the total pressure (=15 cm. Hg) is the partial pressure of oxygen, $\frac{4}{5}$ the total pressure (=60 cm. Hg) is the partial pressure of nitrogen. More generally expressed, the *total* pressure or tension of a mixture of gases is equal to the sum of the *partial* pressures or tensions of the component gases. In the case of air the total pressure (75 cm. Hg) is equal to the partial pressure of oxygen (15 cm. Hg) *plus* the partial pressure of nitrogen (60 cm. Hg). Thus, if the percentage of gas in a mixture is known, the total pressure being also known, the partial pressure of the gas is obtained by a simple calculation. The percentage of oxygen in air being 20, the pressure of air being 75 cm. Hg, the partial pressure of oxygen is $\frac{20 \times 75}{100}$ cm. Hg=15 cm. Hg. The same laws apply to simple solutions of gases in liquids when chemical forces do not intervene, but in the case of blood in which the gases are held in loose combination, their partial pressures cannot be calculated from the percentage, but must be ascertained by direct observation. For example, in blood containing 12 vols O_2 per 100, the oxygen in the absence of chemical force would have a tension or partial pressure $=\frac{12 \times 75}{100}$ cm. Hg=9 cm. Hg; whereas by direct experiment its tension is found to be much lower, *i.e.* about 2 cm.

Hg. Similarly in blood containing 40 vols CO_2 per 100, the CO_2 if simply dissolved would have a tension $= \frac{40 \times 75}{100}$ cm. Hg = 30 cm. Hg; whereas by direct experiment its tension is found to be much lower, *i.e.* about 4 cm. Hg. The explanation in both cases is that the gases are held in loose chemical combination. Thus the blood-gases do not conform to the Henry-Dalton law of pressure, according to which the volume of gas dissolved in a fluid varies directly as the pressure; if pressure is gradually lowered in the blood-pump, the gases are not evolved *pari passu*, their dissociation from the blood at temperatures between 37° and 17° C. does not take place in abundance until the pressure is reduced to between $\frac{1}{3}$ and $\frac{1}{5}$ of its normal value.

The tension of CO_2 in the blood is ascertained by the *aerotonometer*. This in principle is an apparatus in which blood is brought into close relation with two gaseous mixtures in one of which the CO_2 tension is above, while in the other it is below, the anticipated CO_2 tension of the blood. When blood is allowed to dribble through the apparatus it takes CO_2 from the first mixture, and yields CO_2 to the second, and from these data a very accurate estimate of CO_2 tension in the blood is derived. For example, if in the two parts of the tonometer the original CO_2 tension were equivalent to 3 and to 6 cm. Hg respectively, and if by the action of blood on the two mixtures these values were increased to 4 and diminished to 5 cm. respectively, the tension of CO_2 in the blood would be 4·5 cm. Hg.

The CO_2 tension of alveolar air is obtained by the *pulmonary catheter*; this is essentially a double tube, the outer part of which can be dilated so as to block a bronchus, while the inner channel remains in communication with the air beyond the blocked point. The bronchus being blocked a portion of the lung is cut off from ventilation, and the tension of the contained gas soon equalises the maximum tension of gas in the pulmonary capillaries. The CO_2 tension in the alveolar air Wolffberg thus found to be equal to the CO_2 tension in venous blood, and not much greater than that of expired air.

An idea of the relative magnitudes of the O_2 and CO_2 tensions in various situations may be gathered from the subjoined table, principally composed of data supplied by the observations of Wolffberg and of Strassburg on the dog. With reference to these numbers it is to be remarked that they denote magnitudes which are presumably lower than normally exist in the human subject, seeing that the CO_2 of expired air averages 3 per cent. (=2·25 cm. tension) on the dog and 4 per cent. (=3 cm. tension) on man; for blood we have taken in round numbers the tension of 3 cm. Hg as that of CO_2 and of O_2, but as might be expected arterial and venous bloods differ in this respect—representative values are 3 cm. O_2 tension, 2 cm. CO_2 tension in arterial blood, 2 cm. O_2 tension and 4 cm. CO_2 tension in venous blood;[1] as regards alveolar air the value of CO_2 tension given is that of blocked alveoli; the value of O_2 tension is an approximate value of what, judging from the partial pressure of O_2 in the pleural cavity (5·7), presumably obtains in the unblocked alveoli; in blocked alveoli the O_2 tension falls to that of the pulmonary blood, viz. 3 cm.; the difference in the CO_2 tension of alveolar and expired air is not so great as might have been expected—in other words the diffusion of CO_2 is extremely rapid. As regards lymph it is to be observed that the CO_2 tension actually observed is very variable, sometimes exceeding, sometimes falling short of the CO_2 tension in venous blood, and that the O_2 tension is not always at zero; this is attributable to the fact that under the conditions of experiment more or less gas diffuses between lymph and the arterial blood of neighbouring vessels.

Partial pressure of Oxygen and of Carbon dioxide.

	Oxygen		Carbon dioxide	
In atmospheric air . . .	15 cm. Hg		·03 cm. Hg	
In expired air	12 „	↓	2·25 „	↑
In alveolar air	6 „		2·5 „	
In blood	3 „		3 „	
In lymph	0 „		4 „	
In tissue	0 „		6 „	

The passage of oxygen from the atmosphere to the blood and to the tissues, as well as the passage of carbon dioxide from the tissues to the blood and to the atmosphere, can thus be accounted for on purely physical grounds, the incoming current of O_2 and the outgoing current of CO_2 being regarded as ordinary diffusion currents. The diffusion of oxygen is directed from atmospheric to alveolar air, from alveolar air to blood, from blood to tissue. The diffusion of carbon dioxide is directed from tissue to blood, from blood to alveolar air, from alveolar to atmospheric air.

---

[1] If a comparison be made between equal volumes of blood and of serum as regards the amount and tension of CO_2 in each case, it will be found that the amount is greater in serum, but that the tension is greater in blood; all the CO_2 of blood is removable by the gas-pump, but in serum a certain proportion is 'fixed' and removable only after the addition of acid. A pure solution of hæmoglobin will absorb a greater volume of CO_2 than an equal amount of water, and the absorption does not conform to the Henry-Dalton law. From this it has been inferred by Bohr that CO_2 forms a compound with Hb, but no such compound has yet been identified by the spectroscope.

The concurrence of forces other than diffusion has been invoked to account for the discharge of CO_2. It has been shown that the absorption of O_2 is an adjuvant to the expulsion of CO_2, and also that the presence of the N in atmospheric air favours the escape of CO_2; v. Fleischl, moreover, attributes a considerable part to the dissociating effect of the heart's contraction which mechanically assists in the 'liberation' of CO_2; Müller invokes a secretory action of the pulmonary epithelium.

As regards the absorption of oxygen, there can be no doubt that the tissues themselves attract oxygen by virtue of their powerful reducing action. The pressure of oxygen in tissue is maintained at zero, the 'appetite' of tissue for oxygen is so great that not only will it admit oxygen at low pressure, but it will attract oxygen which is held back in chemical combination; thus, living tissue is capable of deoxygenating blood down to the last trace of oxygen; it can even take oxygen from compounds far more stable than oxyhæmoglobin. Of this powerful reducing action we have a striking instance in the effect of living tissue upon alizarin blue. This substance is white in a deoxidised state, blue in the oxidised state. Powerful chemical means are required to reduce it, yet living tissue in or out of the body is capable of so doing; alizarin mixed with minced muscle in a closed vessel will in a few hours lose its blue colour. This effect, be it observed, is not contradictory but complementary of the results of the gas analysis of muscle which only shows that the gasometric method is not suitable to the study of respiratory consumption of oxygen by muscle.

The state of tissue is the determining factor in a chain of events—active respiration of tissue increases the subtraction of oxygen from arterial blood and increases blood-flow through the muscle. Increased blood-flow is thus the consequence and not the cause of increased activity of tissue. And it may be that the acidification, which accompanies muscular contraction and which is known to promote vaso-dilatation, constitutes one of the links between the cause and the effect.

The term 'pressure' is employed so frequently and in so many senses in connection with the mechanism of respiration, that it will be advisable to enumerate and distinguish its various applications: 1. It is used in connection with the pulmonary circulation (blood-pressure). 2. It is used in connection with the pressure of a gas mixed with other gases (partial pressure). 3. It is used in connection with the air-passages (intrapulmonary pressure). 4. It is used in connection with the pleural cavity (pleural or intrathoracic pressure). Pulmonary blood-pressure needs no special explanation; the partial pressure of gases has just been explained. Intrapulmonary and pleural pressures are frequently confused, but should be carefully distinguished from each other; the first is the pressure within the air-passages, it is measured by placing a manometer in connection with one nostril or with a T-tube fixed in the trachea, and it is positive or negative according as the chest is in expiration or in inspiration; the second is the pressure in the pleural cavity; it is measured on the living animal by placing a manometer in connection with a cannula inserted through the thorax and parietal layer of the pleura, and on the dead animal by placing a manometer in connection with a cannula tied in the trachea and then laying the chest open. The pleural pressure is below that of the atmosphere, *i.e.* negative, in ordinary expiration, as well as in inspiration; the only case in which it becomes positive is when an expiratory effort is obstructed; it is the consequence of the elasticity of the lungs, which tend to shrink with more or less force according as the chest is more or less distended; this negative or subatmospheric pleural pressure is least in the expiratory position, greatest in the inspiratory position of the thorax; in ordinary expiration it is − 5 mm. Hg, in ordinary inspiration − 10 mm.; in maximum inspiration − 30 mm. The intrapulmonary pressure varies very little with normal respiration; in ordinary free expiration it is + 2 mm., in ordinary free inspiration it is − 1 mm.; in partially obstructed expiration, as in speaking and singing, it is + 10 to + 30 mm. With completely closed air-passages, an expiratory effort may reach the pressure of + 90 mm., and an inspiratory effort that of − 60 mm. Hg.

Violent expiratory efforts, especially if made against obstruction and frequently repeated, are apt to damage the air-vesicles, the pressure within them may be made so great that they become permanently over-distended and may even be ruptured, giving rise to a condition which is termed 'emphysema.' The lungs of persons who blow wind instruments, and of patients subject to frequent and prolonged fits of coughing, are particularly liable to become thus altered.

Influence of respiration upon circulation.—Respiration affects circulation in three distinct ways; the movements of respiration have a direct mechanical effect upon blood-pressure, they also influence the heart and the blood-vessels through nervous channels, and thirdly the more or less oxygenated state of the blood, brought about by respiration, takes effect upon the vasomotor centre.

Every blood-pressure tracing shows the effect of the respiratory movements; if these be simultaneously recorded with the blood-pressure, it will be found that the arterial pressure rises with inspiration and falls with expiration—the inspiratory rise beginning a little later than the beginning of inspiration, and the expiratory fall beginning a little later than the beginning of expiration. These are mechanical effects of the varying intrathoracic pressure, as will presently be explained.

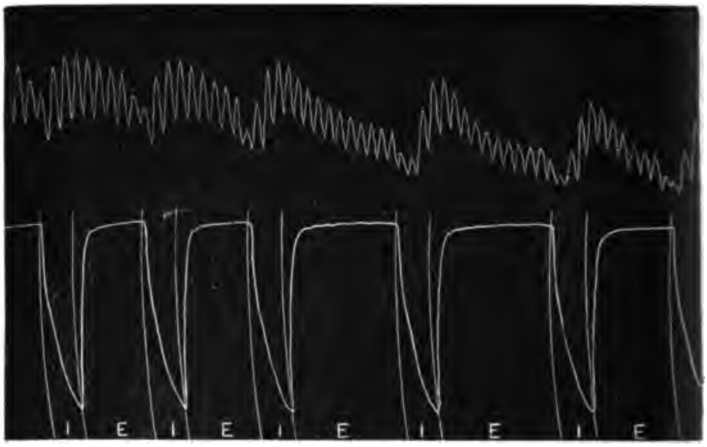


Fig. 59.—Rabbit. Influence of Respiratory Movements upon Arterial Blood-pressure.

The clearest evidence that respiration influences the circulation through nervous channels, modifying the beat of the heart, is furnished by the dog; on this animal the pulse frequency is considerably greater during inspiration than during expiration, a difference which is attributable to the vagi nerves, since it is abolished by their section.

The influence of respiration on the arterial tone is likewise transmitted through efferent nervous channels, and is attributable to the quality and quantity of the blood-supply to the spinal bulb. When the blood is deficient in oxygen, the bulb is stimulated, the vasomotor centre and nerves are excited, and the blood-pressure rises. When the blood-supply of the bulb is obstructed, as by compression of the carotids, the same effects ensue. These effects are equally well produced on an animal with both vagi divided and kept alive by artificial respiration. The excitation of the bulbar vasomotor centre by a deficiency of oxygenated blood cannot endure for any long period; the excitability of its grey matter is soon exhausted if oxygenated blood is permanently withheld; when this occurs the arterioles begin to relax and the blood-pressure falls to and below the normal. This fall which may last one or two minutes is not uniform and continuous, but characterised by undulations of pressure, due to rhythmic vaso-constrictor efforts, the last gasps of the dying vasomotor centre. That these undulations (generally known as the Traube-Hering curves) are certainly due to vasomotor action, and are not mechanical effects of respiratory efforts, is proved by the fact that they occur in the absence of respiratory movements; they are moreover of slower rhythm, not more than two or three per minute, and thereby distinguishable from the mechanical effects of respiration even while these are taking place.

As regards an explanation of the mechanical influence of respiratory movements upon blood-pressure, it is necessary to refer to the mechanical conditions to which the heart and vessels are subject in the thoracic cavity. If the thorax were a freely open cavity, its expansion and contraction could not exercise any pressure on the heart and large blood-vessels; air would simply pass in and out of the cavity. If the thorax were a rigidly closed cavity, *i.e.* if the trachæa were closed, each expansion would diminish the intracardiac pressure, *i.e.* exercise a suction action upon the heart and large vessels; each contraction would increase the intracardiac pressure, *i.e.* exercise a squeezing action upon the heart and large vessels. The thorax may for the moment be regarded as a cavity with a limited outlet, so that its contraction and expansion exercise a slight and temporary plus and minus pressure in the air-passages during expiration and inspiration.

In ordinary expiration the pressure in the air-passages is about 2 mm. of Hg; in ordinary inspiration it is about −1 mm. Hg. These variations of pressure will necessarily be brought to bear upon the blood contained in the intrathoracic vessels, *i.e.* the pulmonary circuit, the heart and the intrathoracic portions of the aorta and of the venæ cavæ. The thick-walled ventricles, and the aorta in which the pressure is high, will not be perceptibly influenced; the pulmonary circuit will be somewhat compressed or relaxed; but the parts which are most affected are the right auricle and venæ cavæ, which are thin-walled and at almost zero pressure.

The elasticity of the lungs is a more important factor, at least in normal respiratory undulations of blood-pressure. As its effect the heart and intrathoracic vessels are not under the full atmospheric pressure of 760 mm. Hg; the air-column does not bear directly upon them, but only indirectly through the distended lung, which by virtue of its elasticity tends to shrink, thereby supporting a certain proportion of atmospheric pressure. The actual air-pressure upon the heart and intrathoracic vessels is therefore subatmospheric, viz. 760 mm. Hg, *minus* the elastic force exercised by the distended lung. The value of this force is about 5 mm Hg in the position of ordinary expiration, and about 10 mm. in the position of ordinary inspiration. So that the heart and intrathoracic vessels exercise a suction of 5 to 10 mm. upon the contents of extrathoracic vessels in the two phases of normal respiration. Taking into account the intrapulmonary pressure of + 2 during expiration, and − 1 during inspiration, the total suction exercised will be − 3 in expiration and − 11 in inspiration.

The thick-walled ventricles and the aorta, in which the blood-pressure is high, will be least influenced by this extravascular variation of pressure, which does not amount to 10 mm. of mercury. The right auricle and the venæ cavæ, which are thin-walled and at almost zero pressure, will on the other hand be sensibly affected by such a variation of pressure, which will practically determine the amount of blood-flow to the right side of the heart. Increased or diminished blood-flow to the right side of the heart rapidly entails increased or diminished blood-flow to the left side, which therefore drives forward a larger quantity of blood soon after inspiration has begun, a smaller quantity of blood soon after expiration has begun. Arterial pressure goes up in the first case, goes down in the second.

The pump action of the expanded lung as just described is no doubt the most effective agent in furthering the flow of blood from the systemic veins to the right auricle, and consequently furnishing the blood which is driven on by the left ventricle; certain special cases have yet to be considered.

In laboured or obstructed respiration the chief varying factor is the exaggerated intrapulmonary pressure, which of course entails a corresponding alteration of the pleural pressure. A forcible inspiration entails a greater negative pressure in the air-passages and in the pleural cavity, a forcible expiration entails a greater positive pressure in the air-passages, and the pleural pressure is now positive instead of negative. These effects are well marked when the respiration is partially obstructed or exaggerated—the great veins at the root of the neck shrink and swell visibly with inspiration and with expiration; the effects are at a maximum when respiratory efforts are made during closure of the mouth and nose—under these circumstances the total inspiratory suction of −11 mm. may be increased to − 70, or taking pleural pressure into account, to −90, and the expiratory suction action of −3 mm. may be replaced by a repulsive action amounting to + 90 mm. Hg. A violent and prolonged inspiratory effort with closed mouth and nose can even cause a temporary arrest of the circulation, the intrathoracic vessels being distended with blood and the auricles unable to contract; this experiment, which is not without discomfort or even danger, is known as Müller's experiment. Conversely a violent and prolonged expiratory effort with closed air-passages is capable of arresting the circulation; the intrathoracic vessels are in this case emptied of blood, and the venous blood from the system is prevented from entering the compressed right auricle; this is known as Valsalva's experiment.

Breathing *compressed or rarefied air* influences the blood-pressure as might be anticipated from the above considerations. Breathing in compressed air lowers the blood-pressure, breathing in rarefied air raises the blood-pressure. If arrangements be made by means of valves, to inspire from rarefied and to expire into compressed air, the normal inspiratory increase and expiratory decrease of blood-pressure will be exaggerated; if on the contrary, inspiration be taken from compressed air, and expiration be made into rarefied air, the normal variations may be diminished, abolished, or even reversed. A man on the top of a mountain breathes rarefied air, in a diving-bell he breathes compressed air, the endurable range of pressure being from a minimum of ½ atmosphere to a maximum of 5 atmospheres, which are the pressures obtained at an altitude of 5,000 meters above sea-level and a depth of 40 meters under water. Death occurred in a balloon ascent reaching 8,500 meters—an altitude at which the pressure is only ⅓ atmosphere. At a pressure of 15 atmospheres animals die in convulsion, at 20 atmospheres germination and putrefaction are arrested, *i.e.* no living cell can breathe. Sudden variations of pressure are far more dangerous than gradual alterations.

In artificial respiration, as ordinarily performed by bellows, the intrapulmonary pressure is increased with inflation, diminished with collapse; the pressure conditions are thus the reverse of those obtaining in normal respiration, and the blood-pressure undulations (provided a moderately slow respiratory rhythm be chosen) are reversed. Each inflation (=inspiration) causes an immediate short rise followed by a more prolonged fall of blood-pressure; each extraction (=expiration) causes an immediate fall followed by a more prolonged rise. These effects are attributable to alterations of air-pressure in the pulmonary alveoli; inflation first squeezes the blood on towards the heart and then retards further blood-flow by compressing the pulmonary capillaries; extraction relaxes the intra-alveolar pressure, it thus momentarily limits the blood-flow and subsequently permits it in greater volume.

These alterations, which are undoubtedly effective in artificial respiration as above described, are probably of some account even in normal respiration; inspiration relaxing the bed, and causing a slight preliminary retardation of blood-flow through the lung, followed by acceleration; expiration compressing the bed, and causing a preliminary acceleration, followed by retardation. But this is at most a very accessory factor in the production of the normal undulations which have been fully accounted for as the consequence of the pumping action of the lungs. Another accessory factor is perhaps of some moment, viz. the compression of the abdominal viscera, more especially of the liver, by the inspiratory descent of the diaphragm; kneading or 'massage' of the abdomen is a ready and effectual means of promoting venous flow, thus raising arterial pressure, and it is possible that ordinary respiration has some action of this kind.

The influence of the respiratory movements upon venous pressure has been incidentally alluded to in the foregoing description, and is easily realised; the familiar fact that the veins shrink with inspiration and swell with expiration is of itself sufficient to remind us of the general rule that variations of venous pressure are in a contrary sense to variations of arterial pressure. This rule holds good throughout all the cases above considered; we may therefore briefly summarise the main effects observed in the venous and arterial pressures—*e.g.* of a carotid artery and of a jugular vein—in the following form.

		Car. press.	Jug. press.
Normal respiration	Inspiration	+	−
	Expiration	−	+
Artificial respiration	Inflation	−	+
	Extraction	+	−

Control of respiration by the nervous system.—The movements of normal respiration are automatic and involuntary, but subject to occasional modification by the stimulation of afferent nerves and by voluntary interference. The nerve machinery consists of (1) a chief respiratory centre in the spinal bulb, (2) afferent nerves, (3) efferent nerves to the muscles of respiration. In its normal automatic mechanism the respiratory centre acts in obedience (1) to the chemical state of the blood as regards the amount of gases, and (2) to the mechanical state of the lung as regards distension. In occasional modifications to which the mechanism is subject, the centre acts in response (1) to exaggerations of its habitual stimuli, (2) to voluntary mandates, and (3) to centripetal stimuli along almost every afferent nerve.

The respiratory centre.—Destruction of the spinal bulb at once arrests the movements of respiration; and, provided the bulb be left intact, destruction of the brain does not abolish these movements. This, of itself, is enough to show that the spinal bulb includes the chief respiratory centre, even though it is not possible to define the centre anatomically as this or that nucleus of grey matter. The most we are able to say with any approach to certainty is that this centre is above the vasomotor centre.

The expression, chief respiratory centre, implies a certain reservation. Observations on animals poisoned with strychnia, more especially on young animals, have been recorded, which prove that imperfect respiratory movements persist after destruction of the bulb; these movements are accepted as evidence that the upper part of the spinal cord in a minor and subordinate

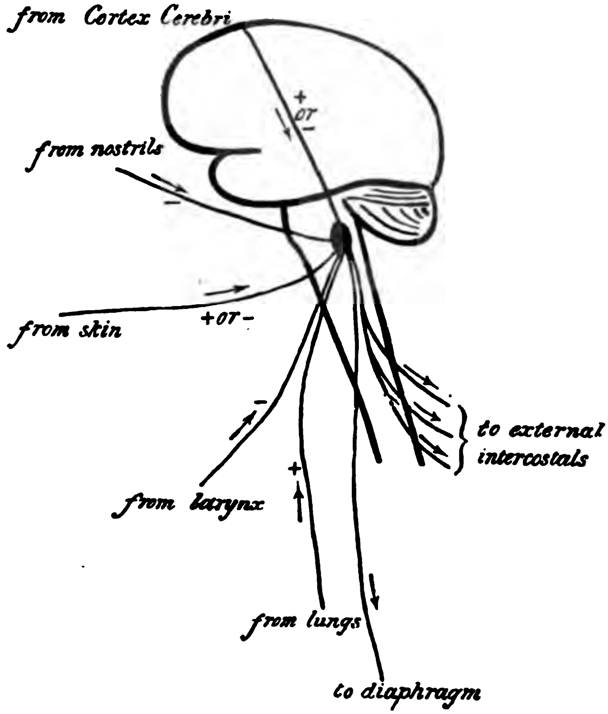


FIG. 60.

Diagram to illustrate the chief nervous connections of the respiratory centre. Impulses may reach it—

(1) From the cortex of the brain (*voluntary control, emotional modifications*).
(2) From the surface of the body (*increase or diminution by cutaneous stimuli*).
(3) From the lung by way of the vagus (*increase*).
(4) From the larynx by way of the superior laryngeal (*diminution*).
(5) From the nostrils by way of the fifth nerve (*diminution*).

Impulses pass from the centre to the diaphragm along the phrenic nerve, to the intercostal muscles along intercostal nerves, and in laboured respiration along many other nerves to many other muscles.

degree takes part in the control of respiration. But this share is less considerable than in the case of vasomotor action, which, as we have seen, while chiefly controlled from the bulb, is also to some extent controlled from the spinal cord. Each lateral half of the bulb is principally concerned in the control of respiratory movements upon the same side of the body.

The respiratory centre is particularly sensitive to the quality of the blood by which it is traversed; its excitability is instantly raised by blood which is deficient in oxygen; it is on the contrary lowered by blood which is fully saturated with oxygen, and in consequence of these alterations of excitability the centre increases or diminishes the energy of respiratory movement. Thus the respiratory supply is a self-adjusting process; ill-oxygenated blood excites respiration and thereby makes up arrears, well-oxygenated blood calms respiration and thereby cuts down excess, the respiratory centre in this relation playing the part of 'blood-taster' to the whole body.

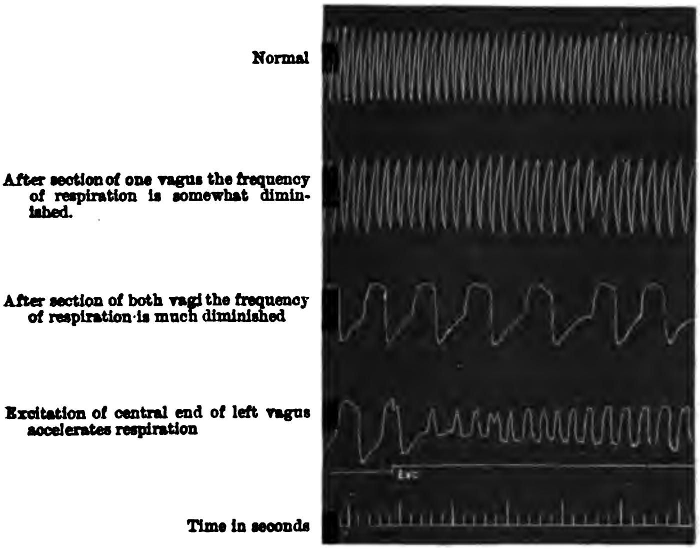


FIG. 61.—INFLUENCE OF THE VAGUS UPON RESPIRATORY MOVEMENTS.

The afferent nerves in most intimate relation with respiratory acts are, in order of importance, the vagus, the superior laryngeal, and the fifth nerve. The vagus appears to be in constant action; the effect of section of both vagi is to render the respiration very slow; excitation of the *central* end of either vagus, if moderate, quickens the rhythm up to and beyond the normal frequency; if excessive, it quickens the respirations to such an extent as to arrest respiration in inspiratory tetanus. These facts show that the vagi are afferent channels of a *plus* influence from the lung which augments respiration. This is the rule, but it is liable to exceptions; one vagus, more often the left than the right, may be the more effective; excitation of the central end of a vagus may sometimes diminish the frequency of respiration instead of increasing it, and lead to arrest in expiration instead of in inspiration; the effects may differ according to the part of the nerve to which excitation is applied. This last circumstance is however intelligible when the effects of stimulating its superior laryngeal branch have been learned. Section of one or both these branches has no effect, but excitation of the central end of either, if moderate, slows the rhythm, if excessive, arrests the chest in expiration. We learn from this that the superior laryngeal may upon occasion transmit a *minus* influence from the larynx which diminishes respiration, and we may indeed recognise it to be natural that irritation of the larynx by a foreign body should suspend the inspiratory, and, it may be, promote the expiratory act. Very similar effects follow excitation of the nostrils, from which the nasal branch of the fifth is the sensory nerve; respiration is diminished, and we may recognise this also as an appropriate effect. These are the three nerves excitation of which gives the most constant results, but the excitation of any afferent nerve may alter respiration, only we cannot always predict whether it will increase or whether it will diminish the act. A dash of cold water to the surface of the body may stop respiration or may start it, so may painful stimulation of the central end of a sensory nerve; but the result may not safely be predicted; the same nerve can 'blow hot and cold;' at most we may expect that weak stimuli will more probably accelerate respiration, strong stimuli more probably arrest respiration.

THE LARYNX.

The lungs form part of the organ of voice, constituting as they do a bellows supplying the blast of air which in consequence of obstructions and resonations in the larynx and in the mouth, furnishes the vibrations of musical tones and of articulate sounds. The voice is produced by the vibrations of the vocal cords influenced by the expiratory blast from the lungs; the articulate sounds of speech are produced by the interruptions and resonations of voice in the laryngeal, pharyngeal, and buccal cavities caused by the tongue and lips. In man and in many animals—dog, sheep, horse, &c.—the voice is usually an expiratory act; other animals such as the cat, pig, and ox, vocalise with inspiration.

The *pitch* of sounds and tones yielded by the larynx depends upon the tension of the vocal cords; with a high-pitched tone the vocal cords are extended, with a low-pitched tone they are shorter and comparatively relaxed. The quality or timbre of the voice is chiefly influenced by resonations in the mouth, nose, and accessory air-cavities.

The larynx consists of a framework of *cartilages* united by *ligaments* and moved by six pairs of *muscles.* The cartilages are the thyroid, cricoid, and two arytenoids; the most important ligaments are the thyro-arytenoid ligaments or true vocal cords; the six pairs of muscles are the crico-thyroid, the lateral crico-arytenoid, posterior crico-arytenoid, the thyro-arytenoid, the inter-arytenoid, and the aryteno-epiglottidean. The *vocal cords* stretch across the top of the larynx from the vocal process of the arytenoid cartilage to the angle of the thyroid rather below the salient point which is seen externally as the pomum Adami. The length of the relaxed vocal cords averages 18 mm. in the male and 12 mm. in the female, and the space or chink between their free edges is the glottis or rima glottidis. The articulation between the thyroid and cricoid cartilages is such that contrac-

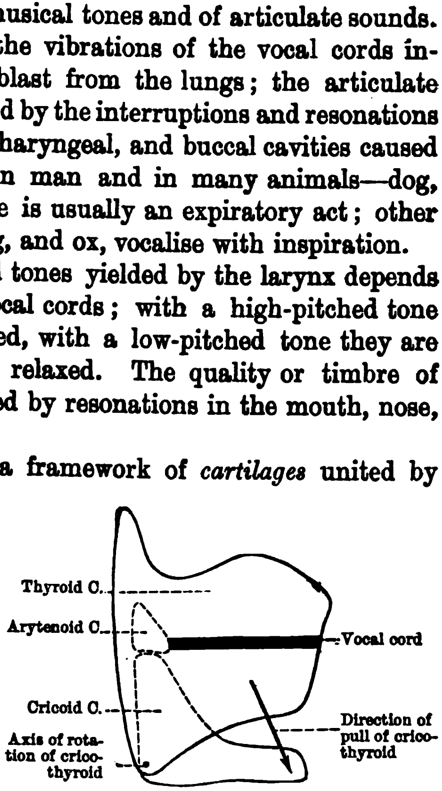

Thyroid C.
Arytenoid C.
Vocal cord
Cricoid C.
Axis of rotation of crico-thyroid
Direction of pull of crico-thyroid

FIG. 62.—DIAGRAMMATIC VERTICAL SECTION OF LARYNX.

tion of the crico-thyroid muscle will tilt the posterior part of the cricoid backwards, or the anterior part of the thyroid forwards, thus stretching and elongating the vocal cords. The articulation between the cricoid and arytenoid is such that the principal movements of an arytenoid cartilage are movements of rotation round a vertical axis, carrying the vocal process and vocal cord towards or from the middle line; these movements of adduction and abduction are effected by the muscles attached to the muscular process of the arytenoid cartilage, viz. the lateral and the posterior crico-arytenoid. These two pairs of muscles are in fact the most important of the laryngeal muscles; the lateral crico-arytenoids rotate the arytenoid cartilages inwards and adduct the vocal cords; they are the muscles most concerned in vocalisation; the posterior crico-arytenoids rotate the arytenoid cartilages outwards and abduct the vocal cords; they act in association with the muscles of inspiration, widening the aperture of the glottis during inspiratory movements. The inter-arytenoid and aryteno-epiglottidean muscles draw the arytenoid cartilages together, and thus effect closure of that portion of the glottis which otherwise remains patent between the two cartilages. The thyro-arytenoid muscles (divisible into an external and an internal portion) have the same general direction as the vocal cords, and in part lie between and in actual attachment to their upper and lower folds; they draw the arytenoid cartilages towards the thyroid, thus relaxing the vocal cords; by their internal portions they are capable of tightening an anterior while relaxing a posterior part of the cords, and it is possible that they may exercise a 'stop' action upon the cords, causing them to vibrate in partial lengths instead of in their whole length.

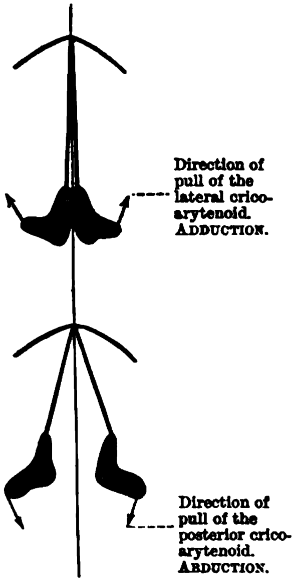
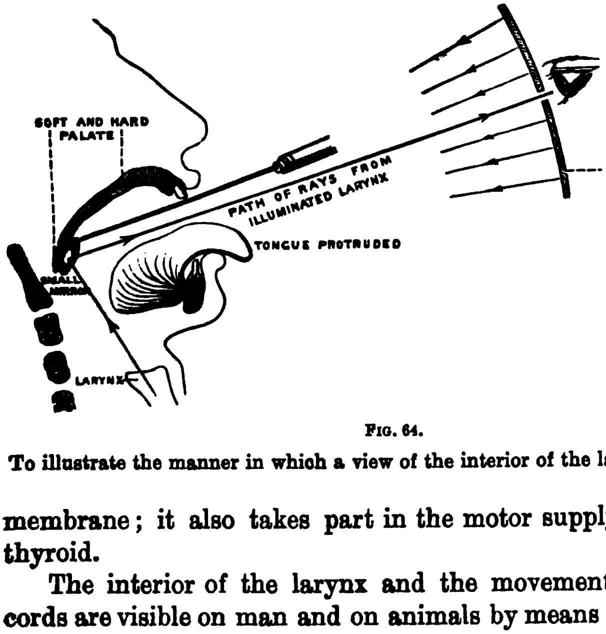

Direction of pull of the lateral crico-arytenoid.
ADDUCTION.
Direction of pull of the posterior crico-arytenoid.
ABDUCTION.

FIG. 63.

Diagrammatic horizontal section through the arytenoid cartilages and vocal cords to illustrate the action of the crico-arytenoid muscles.

The tension of the vocal cords can also be modified by external muscles attached to the thyroid cartilages, more especially the sterno-thyroid and thyro-hyoid; the former depresses the thyroid cartilage and tilts it backwards, thus relaxing the vocal cords; the latter raises the thyroid and tilts it forwards, thus stretching the vocal cords. The inferior constrictor of the pharynx may also assist in relaxing the tension of the vocal cords of a sufficiently flexible larynx by flattening the thyroid cartilage.

The *nervous supply* of the larynx is derived from the superior and from the inferior laryngeal branches of the vagus. The inferior laryngeal is the chief motor nerve of the laryngeal muscles, supplying the lateral and posterior crico-arytenoids, the thyro- and inter-arytenoids, and in part the crico-thyroid. The superior laryngeal is the sensory nerve of the laryngeal mucous membrane; it also takes part in the motor supply of the crico-thyroid.



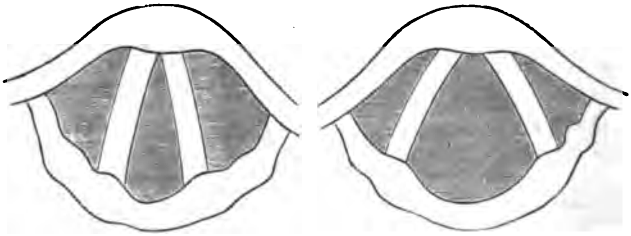
Large perforated mirror, reflecting rays from a lamp which illuminate the larynx. (An unperforated mirror fixed to the forehead answers the same purpose sufficiently well.)

FIG. 64.

To illustrate the manner in which a view of the interior of the larynx is obtained.

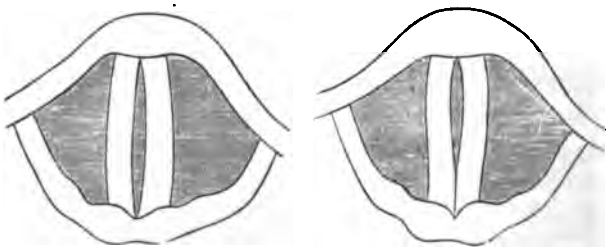
The interior of the larynx and the movements of the vocal cords are visible on man and on animals by means of the *laryngoscope*. This is a contrivance consisting essentially of two mirrors, a larger perforated mirror fixed in front of the eye of the observer, a smaller mirror at the end of a handle by which it can be held at the back of the mouth; the observer looks through the perforated mirror, by means of which he reflects the light of a lamp in the same direction, and inspects a reflection of the interior of the larynx from the smaller mirror held at a suitable angle. The image seen is reversed, the apparent left cord is in reality the right cord, the arytenoid ends of the cords appear anterior, &c. Thus viewed, the vocal cords of a normal larynx are seen to move away from each other during inspiration, and to return towards the middle line during expiration; during the utterance of a sound the cords are seen to come quite close together, the glottis being reduced to a mere chink.

With regard to the position of the cords and consequent shape of the glottis during the singing of notes in different registers, considerable differences of opinion have prevailed, more especially as regards falsetto or head notes. The accompanying figures illustrate the more generally credited view, that the cords vibrate in their whole length in the natural emission of tones, but that they are 'stopped' (by the action of the internal part of the thyro-arytenoid) and only vibrate by their anterior portions during the emission of a falsetto tone.



Position of rest. (The vocal cords are midway between abduction and adduction.)

Position during forced inspiration. (The vocal cords are in extreme abduction.)



Position during vocalisation. ('Chest voice.') The vocal cords are adducted and vibrating in their entire length.

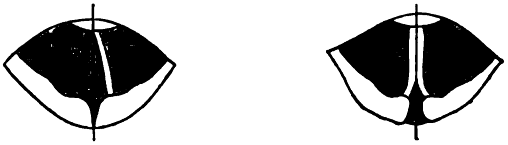
Position during vocalisation. (Falsetto voice.) The vocal cords are adducted and vibrating in their anterior portions only.

Fig. 65.

Diagrams to illustrate the position of the vocal cords under various circumstances.

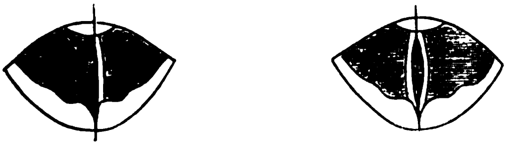
At moments of extreme muscular exertion, when the chest is filled and fixed with an expiratory effort, the larynx is tightly closed; in this closure the false as well as the true vocal cords take part. In a cough as excited by contact of a foreign with the mucous membrane of the larynx, the glottis is closed during the first part of a sudden expiratory effort, and suddenly gives way to the expiratory rush of air.

The consequences of paralysis or of excitation of the laryngeal nerves are in some respects simple, in others peculiar. Clinically as well as experimentally, the commonest form of laryngeal paralysis is caused by section or by compression of the inferior laryngeal nerve; if the nerve of one side be cut or paralysed—say on the right side—the voice is lost (aphonia) because the right vocal cord cannot be adducted, breathing is impeded (inspiratory dyspnœa), because it cannot be abducted; on laryngoscopic examination the right vocal cord neither moves from the middle line with inspiration, nor towards the middle line with vocalisation. It is interesting to note that in a gradually produced paralysis of the inferior laryngeal, it is—contrary to expectation—the abductor or less voluntary muscle, the posterior crico-arytenoid, which fails first, the adductor or more voluntary muscle, the lateral crico-arytenoid, which fails at a later stage; but this order of failure is reversed when function is abolished by an excessive administration of ether.



Paralysis of right abductor or of right inferior laryngeal nerve. Position during inspiration. The right vocal cord fails to be abducted, and remains nearer the middle line than the normal left cord.

Paralysis of inter-arytenoid. Position during vocalisation. The arytenoid cartilages fail to come together, the inter-cartilaginous portion of the glottis remains unclosed.



Paralysis of right adductor, or of right inferior laryngeal nerve. Position during vocalisation. The right vocal cord fails to be adducted, and remains further from the middle line than the normal left cord.

Paralysis of thyro-arytenoid. Position during vocalisation. The vocal cords are not properly stretched, and their edges remain unduly curved.

FIG. 66.

Diagrams to illustrate the chief paralytic defects in the movements of the vocal cords (mirror views).

Strong stimulation of the inferior laryngeal nerve, calling into play all the muscles—abductors as well as adductors—causes closure of the larynx, *i.e.* the adductors predominate; with weak stimulation and during deep etherisation the reverse effect, *i.e.* abduction, is usually obtained.

Paralysis or section of the superior laryngeal nerve abolishes the sensibility of the larynx, and it consequently fails to resent the intrusion of foreign bodies which under normal conditions are expelled by coughing. The voice is rendered hoarse in consequence of deficient action of the crico-thyroid and deficient tension of the vocal cords. Excitation of the central end of the divided nerve produces reflex movements of deglutition and reflex arrest of respiratory movements.

Paralysis of individual muscles produces effects which can easily be deduced from their known physiological action. Thus paralysis of adductors interferes with the expiratory adduction necessary to vocalisation, and causes loss of voice; paralysis of abductors interferes with the inspiratory abduction necessary to free breathing, and causes inspiratory dyspnœa; paralysis of the tensors (crico-thyroid, internal portion of thyro-arytenoid) and of the inter-arytenoids causes hoarseness, in the first case because the vocal cords cannot be properly stretched and approximated, in the second case because the arytenoid cartilages cannot be brought together (see fig. 66).

Paralysis of one side of the brain (hemiplegia) does not affect the laryngeal muscles on either side, the movements of the vocal cords are unimpaired; on the other hand, excitation of one side of the brain sets in action the laryngeal muscles of both sides, the vocal cords are adducted (usually), or abducted (sometimes).

The laryngeal and other nerves concerned in the movements of speech have their spinal centres of origin in the bulb; bulbar paralysis causes, among other consequences, impairment of vocal pronunciation.

CHAPTER V

DIGESTION

PAGE

156 Physiological anatomy of the digestive tube.

157 The general drift of digestion.

THE DIGESTIVE MOVEMENTS

159 Mastication—Deglutition: its three stages; time-relations; sounds; nervous mechanism.

163 Gastric and intestinal movements; peristalsis; influence of nerves, of blood, of drugs.

164 Defæcation—Vomiting.

THE DIGESTIVE FLUIDS.—I. SALIVA

166 Composition of saliva—Microscopical appearance—Uses and properties—Experiment.

169 Structure of salivary glands—Mucous and serous—* Changes of structure consequent upon activity—Mammary secretion.

175 Other physical changes associated with salivary secretion -Heat—CO_2.

175 * Influence of the nervous system upon secretion—Independence of secretory nerves; pressure proof, post-mortem proof, atropin proof—The chorda tympani is secreto-motor; the sympathetic is secreto-motor—Reflex salivary secretion—The submaxillary ganglion.

179 Particular kinds of saliva—Sympathetic saliva—Cerebral saliva—Paralytic saliva—Exhaustion saliva.

180 Effect of drugs—Atropin and pilocarpin.

II. GASTRIC JUICE

181 Physiological anatomy of the stomach—Alterations of structure with activity.

183 Composition and properties of gastric juice—Nature of the gastric acid.

184 Action of gastric juice—Experiment—Brücke—Meissner—Kühne.

187 Pepsin; its source—Pepsinogen—Estimation of pepsin—*Grützner's method—Other ferments.

189 Influence of the nervous system.

190 Gastric fistula—Gastric cæcum—Self-digestion post-mortem.

191 Classification and identification of proteids—Albumose.

III. BILE AND PANCREATIC JUICE

PAGE
196 Physiological anatomy of the liver and pancreas.
197 Bile—Composition, properties, and tests—Pancreatic juice; ferments.
200 Uses of the bile—Secretion and excretion—Association of bile with pancreatic juice
202 Experiments on fats, on proteids, and on starch.
204 Bile-acids and bile-pigments are made by the liver—Deposition of iron.
206 Biliary secretion—Biliary pressure.

INTESTINAL ABSORPTION

208 Physiological anatomy of the small intestine—Structure of a villus.
210 Intestinal juice: Characters and properties—Thiry-Vella fistula—Moreau's experiment.
211 Absorption by blood-vessels and by lymphatics—Epithelial activity.

* GLYCOGENESIS

213 The glycogenic function of the liver: Bernard's discovery—Objections—Source of glycogen.
216 Characters of and tests for glycogen—Its preparation.
217 Influence of diet, of health, of exercise—The sugar cycle—Carbohydrate reserve.
218 Alterations of liver structure by feeding.
219 Diabetes.

Physiological anatomy of the digestive tube.—The digestive tube is lined internally by mucous membrane, externally by muscle, and receives the ducts of several tributary glands (salivary, hepatic, and pancreatic). The mucous membrane is the channel of absorption and of secretion, the muscular coat supplies motor power by which solid food is broken up and propelled along the canal. In the greater part of its length and excepting more particularly at its two extremities (mouth and anus), the muscular coat of the tube is composed of involuntary smooth fibre disposed in two layers, internal circular and external longitudinal, between which there is a close plexus of non-medullated nerve-fibres and ganglion-cells, the myenteric or Auerbach's plexus. The mucous membrane differs in different segments; from œsophagus to rectum it has a layer of smooth muscle (*muscularis mucosæ*) as one of its constituents, and it is separated from the muscular coat proper by a submucous connective-tissue coat, in which are contained the ramifications of blood-vessels, lymphatics, and nerves, the latter forming a loose plexus of non-medullated fibres and ganglion-cells (the plexus of Meissner). In the mouth and in the œsophagus the epithelium of the mucosa is stratified, in the stomach it is beset with branched tubular glands, in the small intestine with simple short tubular glands (Lieberkühn's) and with projections (villi), in the large intestine with long tubular glands; at the anus stratified epithelium again appears. The mucous and submucous coats contain moreover a large quantity of lymphoid tissue, especially at the tonsils, in the lower half of the small intestine (Peyer's patches) and in the large intestine. The greater part of the abdominal portion of the tube is covered externally by a serous coat formed by peritoneum. The terms 'inner' and 'outer' are used with reference to the tube itself; the tube is however an involution of the external surface, so that physiologically, with reference to the body-mass, the epithelium of the mucous membrane is the true external surface.

The mucous membrane of the tongue is beset with variously shaped projections or papillæ, anatomically distinguished as filiform, fungiform, and circumvallate. The latter, confined to the posterior part of the tongue, are each surrounded by a circular trench on the sides of which the so-called '*taste-buds*' are found. These are small ovoid bodies composed of long cells into which nerve-fibres have been traced; they are supposed to be gustatory in function, although the fact has not actually been proved. The substance of the tongue is striated muscle, the fibres of which are of small diameter and branched. The muscles of the lips, cheeks, palate, and pharynx are of the ordinary skeletal character.

The teeth are composed of dentine, surrounding a cavity which contains the 'pulp;' the exposed portion or crown of the tooth is covered by enamel, the embedded part or root by cement; vessels and nerves and lymphatics ramify in the pulp, the mass of which consists of lymphoid tissue.

The general drift of digestion.—'*Food*' includes the following classes of proximate principles—*proteids*, *carbohydrates*, *fats*, *salts*, and *water*. Of these, the last two—viz. salts and water—can pass unaltered into the animal body by simple *diffusion* through any part of the mucous membrane; they do not require to be digested. Food belonging to either of the first three classes cannot pass unchanged; it requires to be altered before it can pass into the body. This necessary change is, properly speaking, *digestion*, and it is carried on at the surface of the digestive tract, more particularly in the stomach and in the small intestine. We recognise then that digestion is a preparatory process by which food in the digestive tract, though not yet in the body, is altered and rendered capable of being absorbed, and we commonly include in the process this, its last step, viz. *absorption*, or the actual passage of the digested food through the epithelium of the mucous membrane into the underlying chyle and blood-vessels. Before absorption, food is outside the body, though in the intestinal tube, undergoing digestion; after absorption, it is in the body forming part of the nutritive fluids, blood and lymph. We may, indeed, by analogy with the process of respiration, speak of digestion as an external process—a transaction between the contents of the intestine on one side and the blood and lymph on the other. Food in the intestine is acted upon by juices derived from the blood, by the series of secretions poured out by the glands in the walls of the digestive tract, and by glands (the pancreas and the liver) the ducts of which open into that tract. These secretions are—saliva, gastric juice, bile, pancreatic juice, and intestinal juice, and their respective shares in the entire process are as follows. Proteids are digested by the agency of gastric and of pancreatic juice; fats are digested by the agency of bile and of pancreatic juice; starch by the agency of saliva and of pancreatic juice; cane-sugar by the agency of intestinal juice. In all these cases (except in that of cane-sugar) the effect of digestion is to transform indiffusible into diffusible bodies, and thus facilitate their absorption. But that absorption is not physically identical with diffusion, is illustrated by the case of cane-sugar, which although highly diffusible does not pass unchanged, and by that of fat, which in part at least can pass, although not strictly speaking diffusible. We recognise then that the absorption of digested matter depends upon two conditions—firstly, a physical condition—the diffusibility of the digested material; secondly, a physiological condition—the selective activity of the epithelium through which absorption is effected. The essential constituent of each digestive fluid is a *ferment*—*ptyalin* in saliva, *pepsin* in gastric juice, *trypsin* in pancreatic juice, *invertin* in intestinal juice. These and other ferments are the specific agents by which the digestive transformations of food are effected. They are the occult agents of modern physiology, inasmuch as they have never been isolated as definite bodies, and are recognised to be present only by the effects they produce.

The chemical action of the digestive fluids is promoted by mechanical assistance; each mouthful of food is subdivided by *mastication*, and propelled into the stomach by *deglutition*; the swallowed mass is churned and well mixed with gastric juice by the muscular action of the stomach-wall; reduced to pulp ('chyme'), it is squeezed through the pylorus and propelled onwards along the intestinal tube by *peristaltic contraction*; finally what is left of it—the refuse which has not been absorbed—together with a small proportion of actual excretion from the intestinal tube, accumulates in the rectum, and is discharged by the movement of defæcation.

THE DIGESTIVE MOVEMENTS

Mastication.—Each mouthful of solid food requires to be reduced to a more or less minutely subdivided state by chewing. This state is of great importance to subsequent digestion by facilitating the free access and admixture of the digestive juices with the food; considerable lumps of food may indeed be disposed of by persons having a 'good digestion,' but in weaker and especially in old persons, a hurriedly swallowed meal is apt to be followed by indigestion, and bad teeth are a fruitful source of dyspepsia, *i.e.* difficult digestion, simply owing to the fact that imperfectly chewed food is digested with difficulty.

Each person possesses during life two complete sets of natural teeth—a first or temporary set, the milk-teeth, appearing during the first two or three years of life, and being displaced by a second or permanent set, which begin to make their appearance about the sixth year. The milk-teeth are twenty in number and comprise eight incisors or cutting teeth, four canines or tearing teeth, eight molars or grinding teeth. The permanent teeth are thirty-two in number, and comprise eight incisors, four canines, eight premolars or bicuspids, and twelve molars. A comparison of the skull and teeth of man with those of a purely carnivorous animal, such as the tiger, and with those of a purely graminivorous animal, such as the ox, leads to the conclusion that a mixed diet comprising flesh and vegetables is natural to man. A comparison of their intestines leads to the same conclusion; the intestine of a flesh-feeder is short, that of a vegetable-feeder is long, that of a man is of moderate length.

Deglutition.—A mouthful of food having been masticated and mixed with saliva, is collected by the muscles of the lips, tongue, and cheeks, into a rounded mass or 'bolus' which glides over the base of the tongue into the pharynx, where it is grasped and passed onwards by the action of the constrictor muscles, to the œsophagus, along which it is forced into the stomach by a succession of muscular contractions. The act of deglutition is thus divisible into three stages, 1. *buccal*, 2. *pharyngeal*, 3. *œsophageal*. Of these the first or buccal stage is entirely voluntary; so long as the bolus has not passed through the isthmus of the fauces it may be rejected if desired; once past the isthmus it cannot be turned back.

The second or pharyngeal stage is an involuntary and highly complicated reflex act composed of several distinct movements, which concur to close the superior orifices of the pharynx, and to prevent the food or liquid from returning to the mouth or penetrating to the nose or larynx. This result is effected by, 1. contraction of the pharynx, the muscles of which grasp the bolus; 2. contraction of the isthmus of the fauces, shutting off the buccal from the pharyngeal cavity; 3. elevation of the larynx and occlusion of the glottis; 4. elevation of the velum palati and occlusion of the posterior nares, shutting off the nasal from the pharyngeal cavity. The shape and position of the epiglottis are such as to suggest that it might act as a lid covering the superior orifice of the larynx during the second stage of deglutition. On closer examination it is seen that the epiglottis gives no such protection, and that it may be lost without loss of protection; it is because the larynx is raised and the base of the tongue thrust backwards, that food and liquids do not normally find access to the windpipe. The state of the orifices of the Eustachian tubes during the second stage of deglutition has been debated; it is probable that these orifices are closed during inaction of the pharynx, and opened during the second stage of deglutition; hence the usual practice of inflating the tympanum by forcing air through the nostrils while the patient is in the act of swallowing.

The third or œsophageal stage completes the act of deglutition. The contraction, which is an involuntary one, is of an apparently 'peristaltic' character; that is to say, it is a slowly progressing wave of constriction. It is remarkable, however, that the wave is not arrested by section or ligature of the œsophagus, whereas it is arrested by section of the œsophageal nerves. (Mosso.) These facts show that the apparently peristaltic wave is the expression of a sequence of action occurring in the nervous centre with which the œsophageal nerves are in functional connection, and not a true wave of contraction along a continuous sheet of muscle. Stimulation by the passage of swallowed food or saliva, is required to produce the contraction, which is therefore reflex in character. When experimentally excited, the contraction can only travel from above downwards, and never in the reverse direction; but the phenomena of rumination and vomiting are significant of the possibility of a reversed order of progression when contraction occurs under peculiar physiological conditions.

Time relations.—The time relations of a complete act of deglutition are on man as follows. Taking the contraction of the mylo-hyoid as the point of departure,

the contraction of the pharynx commences	0·3	sec. later
that of the upper part of the œsophagus „	1·2	„
„ middle „ „ „	3·0	„
„ lower „ „ „	6·0	„

and (corresponding with the fact that on man the upper part of the œsophageal muscle is striped, the lower part smooth, and the middle part mixed) the duration of the contraction is in the first part 2 to 2·5 seconds, in the second part 6 to 7 seconds, in the third part 9 to 10 seconds. In the dog's œsophagus, which is of striped muscle throughout, the contraction has in all parts a duration of between 1 and 2 seconds.

Sounds caused by deglutition.—On auscultation of the œsophagus of man during the deglutition of fluid, two distinct sounds are audible—the first practically simultaneous with the commencement of the act, the second about 6 seconds later. The first (which is not always to be heard) is attributable to a squirt of liquid down the œsophagus; the second (which can nearly always be heard) is probably due to the peristaltic contraction of the œsophagus squeezing the fluid through the cardiac orifice of the stomach. Kronecker and Meltzer have shown that if a series of voluntary acts of deglutition are made at intervals of a second, it is not until the last of these that a peristaltic contraction of the food-tube is produced. Each act of deglutition interferes with the natural consequence of the preceding act which should have led to a peristaltic contraction, and it is probable that the glosso-pharyngeal nerve is the afferent channel of this peculiar form of arrest. In the passive state the cardiac end of the œsophagus is semi-contracted; it relaxes during the last part of deglutition, and contracts more firmly after the conclusion of the act.

Nervous mechanism.—Deglutition, after completion of the buccal stage, is a well-characterised and definite reflex act. It is not possible to swallow without something to swallow; and it is the contact of food or of liquid with the anterior surface of the soft palate, which supplies the necessary stimulus, the afferent channel being the fifth nerve; it may also be accidentally as well as experimentally provoked by excitation of the mucous membrane of the larynx, or of the superior laryngeal branch of the vagus. A third channel through which the reflex act of deglutition is influenced, but in an opposite sense, is the glosso-pharyngeal nerve; an act of deglutition experimentally excited by stimulation of the central end of the superior laryngeal or by irritation of the soft palate, fails to take place during excitation of the central end of the glosso-pharyngeal, thus showing that the last-named nerve exercises a centripetal inhibitory effect on the stimulus. The centre from which the movements of deglutition are governed, is situated in the upper part of the spinal bulb; destruction of the brain above, or abolition of its function, does not interfere with deglutition; on the other hand, difficulty of deglutition is one of the symptoms of disease of the medulla oblongata ('bulbar paralysis'). The efferent channels are the motor nerves to the various muscles concerned—viz. the hypoglossal (to the tongue), the facial (to the mylo-hyoid), the glosso-pharyngeal, vagus and accessory (to the muscles of the pharynx, œsophagus, and palate). As has been already mentioned. the orderly contraction of the muscular tube from throat to stomach is regulated in the bulbar centre, not being interrupted by section of the œsophagus.

An experiment by Goltz is often quoted to show that the vagi nerves counteract tonic contraction of the œsophagus. The experiment is as follows:—Two frogs are hung up, one with the vagi intact, the other with both vagi cut or simply pithed. The hearts of both are removed. Salt solution is poured into their mouths. The œsophagus and stomach of the first frog are soon distended with fluid, those of the pithed frog remain obstinately contracted. In other words a viscus from which nervous influence is removed, remains in tonic contraction, while a viscus which is still under control of the nervous system yields to the pressure of fluid. . In mammals, however, the vagus (by fibres derived from the spinal accessory) acts as a motor nerve upon the pharynx and œsophagus ; if it is paralysed, deglutition is interfered with, and food accumulates in the œsophagus.

Gastric and intestinal movements.—The movements of the stomach and of the intestines are undoubtedly peristaltic in nature. Those of the stomach are of a complex churning character; those of the small intestines afford the typical example of *peristaltic* contraction, *i.e.* a prolonged contraction slowly advancing along the muscular tube, in the form of an annular constriction, travelling along the contractile substance as a wave which is directly transmitted from part to part, independently of excitation through nerves. The peristaltic wave of the small intestine is thus fundamentally different from the so-called peristaltic wave in the œsophagus ; the former requires only muscular continuity, and will persist after severance from the central nervous system ; the latter, as stated above, persists after section, but fails after its nerves have been severed ; moreover the œsophageal contraction caused by local stimulation can only travel downwards, while the intestinal wave can travel in either direction, although normally it always travels downwards.

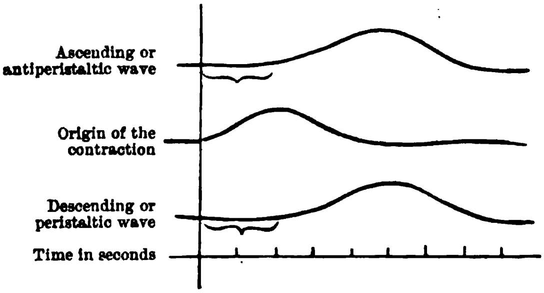


FIG. 67.

Wave of peristaltic and of antiperistaltic contraction in small intestine of dog. After Engelmann. The records were taken 5 cm. above and below the origin of the contraction ; the wave travelled this distance up or down in about 2 sec.,*i.e.*, at the rate of 25 mm. per second.

Influence of nerves.—The activity of intestinal movements, although not directly dependent upon, may be influenced by nerves ; it is also modified by the state of the blood, by the nature of the chyme, and by drugs. The nerves which influence peristaltic movements are the vagus and the abdominal splanchnics. Section of any or of all these nerves causes no very obvious effect, intestinal movements continuing as before, being, if anything, more active in consequence of the vascular engorgement which is produced by section of the nerves. If, while the intestines are in active movement, the peripheral end of thè splanchnic be excited, the movements will be arrested. If, while the intestines are quiescent, the peripheral end of the vagus be excited, movements will be provoked; but it must be added that the same effect is not seldom produced by excitation of the splanchnic. These results, although not so clear and decisive as might be wished, are nevertheless admitted as evidence that the vagus excites, while the splanchnics inhibit intestinal movements. It is to be observed that in experiments of this nature, the intestines must not be freely exposed to excitation by cold air, but should be protected by immersing the animal in a warm bath of normal saline.

So long as the intestine is properly supplied with oxygenated blood, it remains comparatively quiescent; as soon as the oxygen supply is interfered with, the intestines begin to move. This interruption of the oxygen supply can be caused in different ways, by dyspnœa with resultant venosity of the blood, by sluggish or failing circulation and consequent venous engorgement of the visceral blood-vessels, by anæmia of the intestine in consequence of the vaso-contrictor action of the splanchnic nerves. Any of these causes may excite the intestines to exaggerated movements, which are thus among the signs of failing circulation—in a fainting fit, or at the approach of death.

In the normal state of health, intestinal movements are quietly effected without arousing consciousness, but if the intestinal contents be abnormal in quality or consistence, the intestine may move too weakly or too strongly and make its presence felt. This is one among other proofs that the intestinal nerves contain afferent fibres.

Sluggish intestinal movements may be stimulated by purgative drugs, excessive intestinal movements may be controlled by sedative drugs. The consideration of these matters belong to practical medicine rather than to experimental physiology and it will suffice to mention in this place drugs the actio of which has been most studied by experiments involving direc observation of intestinal movements, viz. morphia and belladonna, which exercise a direct sedative action; muscarin, colocynth, and purgative salts, which on the contrary excite intestina movements as well as intestinal secretion.

Defæcation is a reflex act which can be initiated or r sisted by voluntary action. The normal excitant of the act the presence of fæces in the rectum; the normal consequence of the excitant is the orderly sequence of movements termed defæcation. These movements comprise:

1. Contraction of the rectum and of the abdominal muscles.
2. Contraction of the levator ani and of the sphincters.

A distended rectum is an excited and contracting rectum, it causes in consciousness a desire to defæcate. The voluntary response to this suggestion may be 'yes' or 'no;' 'yes' taking the form of contraction of the abdominal muscles with a passive condition of the sphincters, or 'no,' contraction of the sphincters with a passive condition of the abdominal muscles. In this latter case the desire is resisted, and the contracting rectum drives back its contents into the sigmoid flexure. In the former case, the desire is satisfied by a normal act of relief, which commences with contraction of the rectum and of the abdominal muscles, and ends by contraction of the levator and sphincter ani. The foregoing analysis applies to the normal state in which the excitant is of moderate degree, and when it is possible to choose between the two alternatives. It may happen, however, (1) that the excitant is excessive, the desire imperative, the voluntary negative insufficient to arrest the act: such a condition is termed incontinence of fæces or diarrhœa; (2) that the excitant is deficient, the desire absent, the voluntary affirmative insufficient to commence the act: such a condition is termed 'constipation.'

The rectum and the anal muscles are supplied by the hypogastric and erigentes nerves; in the dog these nerves take origin from the spinal cord on a level with the 5th, 6th, and 7th lumbar vertebræ, to which region the term *ano-spinal centre* has accordingly been applied. The nervous mechanism of defæcation is closely analogous with that of micturition. (See p. 243.)

Vomiting is a border-land phenomenon between the normal and the abnormal events occurring in the living body. In ruminating animals the return of food from the stomach to the mouth is a regular event; in infants the act of vomiting follows the most trifling causes, and is effected with the greatest ease; in adults it is an accident which may be caused by irritation of the stomach or indeed by irritation of any viscus; the horse and the rabbit, in consequence of the anatomical disposition of the cardiac orifice, cannot vomit. As regards its nervous mechanism, the act itself is a reflex; its afferent channels are the afferent nerves from the seat of irritation (palate, fauces, stomach, uterus, intestine, liver, kidney, brain); its efferent nerves are the motor nerves of the stomach, of the diaphragm, and of the abdominal muscles; its centre—the so-called vomiting centre—is situated in the spinal bulb. As regards the muscular mechanism of the act, it is effected by simultaneous contraction of the abdominal muscles and of the stomach; the pyloric orifice is firmly closed, the cardiac end of the œsophagus is relaxed, and the contracting stomach is at the same time compressed by the diaphragm and by the abdominal muscles; its contents are thus driven up the œsophagus and ejected through the mouth or nose. By experiments on animals it has been shown that the contraction of the stomach alone, or of the abdominal muscles alone, is sufficient to accomplish this ejection, for it can be completed by the stomach alone after section of the phrenic and intercostal nerves, or by the abdomen alone after the stomach has been excised and replaced by a bladder. In man, as has probably been experienced by most people, vomiting is preceded by a feeling of nausea, by a copious flow of saliva, and by preliminary 'retching' efforts which have the effect of opening out the food-tube by distending it with air.

Drugs which cause vomiting are called *emetics*; their action may be either local, by excitation of the pharynx, œsophagus, and stomach, or general, by excitation of the spinal bulb through the medium of the blood into which an emetic has been absorbed. The popular remedy, mustard and water, is an instance of an emetic acting by local excitation; apomorphine on the other hand is an emetic by its action on the bulb after it has been absorbed or injected into the circulation.

THE DIGESTIVE FLUIDS

I. SALIVA

Its composition.—Ordinary saliva in the mouth is a mixture composed of the secretions of the parotid, submaxillary, sublingual, and small buccal glands. The average daily secretion amounts to 1½ litre. Its reaction is alkaline. It has a specific gravity of about 1,005. It is composed of water, salts, mucin, serum-albumin, and serum-globulin; it contains a ferment (ptyalin), and in solution a gas (carbon dioxide). Serum-albumin and serum-globulin are principally contained in the parotid secretion, mucin in the submaxillary and sublingual secretions; ptyalin exists in the secretions of all these glands in man, but in animals the fermentative effects on starch of different kinds of saliva is very variable. Thus the parotid secretion is very active in the case of the rabbit (contrasting with the submaxillary of the same animal which has little or no action), quite inactive in that of the horse, and only slightly active in that of the dog.

The chief salts present in saliva are sodium chloride, calcium carbonate and phosphate (the two latter salts are apt to form concretions as 'tartar' on the teeth, and 'salivary calculi'), and (frequently but not always) sulphocyanide of potassium; it is remarkable that so poisonous a salt should be found, even though only in minute quantity, in normal saliva; a red coloration on the addition of ferric chloride is the test of its presence. The only gas present in quantity in saliva is carbon dioxide—100 c.c. of saliva containing as much as 60 c.c. of CO_2; only minute amounts of oxygen and of nitrogen are present, not sensibly more than in ordinary water.

A drop of saliva examined under the microscope is seen to contain a few squamous epithelial cells (which are derived from the mucous membrane of the mouth), 'salivary corpuscles,' and perhaps fragments of food and bacteria. None of these things are specially characteristic of saliva; they are only accidental impurities; the 'salivary corpuscles' themselves are simply escaped leucocytes, probably derived from the lymphoid tissue of the tonsils and of other parts.

Its uses and properties.—The uses of saliva are mainly mechanical, and in small degree chemical. Saliva is necessary to adequate mastication and to deglutition; neither of these acts can be effectually performed with the mouth dry; the fluid is equally necessary to adequate articulation, and the sense of taste depends upon saliva to this extent, that before any solid substance can be tasted, it must be in part dissolved, saliva acting as the solvent if no fluid is taken into the mouth. The chemical action of saliva is the conversion of *starch* into *sugar* (maltose), and this conversion is brought about by the salivary ferment, *ptyalin.* That the conversion is effected by a ferment is at once proved by comparing the action of boiled with that of unboiled saliva; boiled saliva does not convert starch into sugar. The conversion by normal saliva is not immediate nor is it complete. It is not immediate—starch acted upon by saliva passes through a series of *dextrins* before sugar is produced; among these are distinguished *erythrodextrin* and *achroodextrin.* It is not complete—the sugar produced does not reach an amount corresponding to the original amount of starch, however long the action is allowed to continue.

Experiment.—A mixture of soluble starch and saliva is allowed to digest at a temperature of 35° to 40°, and tested from time to time. Soluble starch gives a blue colour with iodine solution which disappears on heating and returns on cooling. The digest of starch and saliva soon loses this reaction, and a sample of the mixture gives a red colour, which disappears on heating and does not return on cooling; this red colour indicates the presence of erythrodextrin. A little later the same test gives no colour, while the test for sugar does not yet give evidence of the presence of sugar; at this stage dextrin is present giving no colour with iodine, viz. achroodextrin. Later still sugar is formed in greater and greater abundance; a sample of the mixture boiled with a drop or two of copper sulphate and excess of caustic potash, gives a red or yellow precipitate of copper suboxide, indicative of the presence of a reducing sugar; at this period, sugar (maltose) and dextrin (achroodextrin) are present, and, however long the digestion be continued, dextrin continues to be present; the sugar produced is a reducing sugar, most nearly resembling, though probably not identical with, maltose. We have in the above experiment distinguished the following stages:—

		Tests
1. *Initial substance.*	Soluble starch.	Blue with iodine.
2. *Intermediate substances.*	Dextrins (including erythrodextrin).	Red with iodine.
3.	Dextrins (achroodextrin).	No reaction with iodine. No sugar reaction.
4. *Final product.*	Dextrins and sugar.	Yellow ppt. of Cu_2O on boiling with $CuSO_4$ and KHO.

The chemical equation which most nearly represents the whole process is—

$$\underset{\textit{Starch}}{10\,(C_{12}\,H_{20}\,O_{10})} \underset{}{+} \underset{\textit{Water}}{8\,H_2O} = \underset{\textit{Maltose}}{8\,(C_{12}\,H_{22}\,O_{11})} + \underset{\textit{Dextrin}}{2\,(C_{12}\,H_{20}\,O_{10})}$$

i.e. the process is one of 'hydration' or assumption of water by starch under the influence of the ferment.

The character of action of the salivary ferment is further defined by experiments showing, 1. that it is destroyed by boiling,

2. that its action is delayed or suspended at a low temperature, most pronounced at about body temperature (37°), 3. that it acts best in a neutral or in a faintly alkaline medium, not at all in an acid medium or in too strong an alkaline medium, 4. that it has almost indefinite power, if the product of its action (sugar) is not suffered to accumulate. In all these respects (with the exception of the third), the salivary ferment resembles ferments in general, which are destroyed by heat, delayed by cold, and are limited in their action only by the accumulated product of such action.

Structure of salivary glands.—All the salivary glands are of the compound racemose type, their branching ducts terminate—or rather commence—in groups of short tubes, the *acini*, which are lined by cubical or spheroidal epithelium. Two chief types of gland are distinguished—(a) *serous*, of which the parotid is the representative, and which yields a watery secretion containing serum-albumin as its principal constituent, (b) *mucous*, of which the dog's submaxillary is the chief representative, and which yields a more viscid secretion containing mucin. As usually seen in stained sections the two varieties are recognised by the greater size of the acini and of the cells by which they are lined, and by the clearness of these cells in mucous glands, as compared with the smaller acini, smaller and more granular cells obscurely separated from each other, which are characteristic of serous glands. Another noteworthy point of distinction is the presence in mucous glands of the so-called *crescents* or *demilunes*, which are groups of young cells crowded in between the fully developed mucous cells and the basement membrane upon which they are set; these crescentic masses stain deeply with logwood or carmine. The ducts of the salivary glands are recognisable by their large lumen and by their lining epithelium; in contrast with the clear mucous or the small granular serous epithelium of the alveoli, the cells lining the ducts are regularly columnar, exhibiting in section a granular zone surrounded by a striated zone contiguous with the basement membrane of the duct. With regard to the termination of nerves in the gland-cells, while we cannot doubt from the results of experiments that nerves do communicate with the secreting cells of the alveoli, yet we are constrained to admit that all attempts at microscopic demonstration of the junction have been unconvincing.

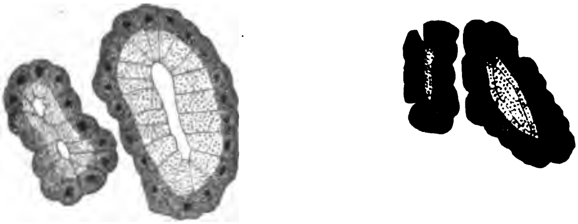
Glands of the same name have by no means the same structure in all animals, nor is a salivary gland necessarily entirely 'mucous' or entirely 'serous'; it may be 'mixed,' *i.e.* serous in some parts, mucous in others; and even a single alveolus may contain individual serous and mucous cells side by side. The submaxillary of man is an instance of such a mixed gland, whereas in the dog and cat it is entirely mucous, and in the rabbit entirely serous. The parotid does not, however, seem to vary from its regular type, which is that of a serous gland in all animals.

Changes of structure consequent upon activity.—The microscopic appearances of the salivary glands differ greatly according as they have been at rest or in activity just before their removal. In both serous and in mucous glands alike, the acini and the cells are shrunken in the active as compared with the rested gland; the active gland has obviously expended some of its substance, as indeed is evident by comparing the entire gland of the fatigued side with the gland of the opposite side, which has been left at rest; the former is the smaller and lighter of the two.

To appreciate in detail the microscopic differences between these two contrasted states, it is necessary to bear in mind what kind of preparation for microscopical examination has been adopted, and whether a given description refers (a) to alcohol-hardened gland stained by logwood or by carmine, or (b) to gland examined during life or freshly teased out in salt solution.

Comparing carmine-alcohol preparations of a serous gland, (such as the pancreas of the dog), it is observable that the cells lining the acini of the resting gland are marked by two distinct zones:—1. an outer stained all but homogeneous zone, 2. an inner unstained and granular zone—whereas after prolonged action the second zone is much diminished, the first zone is increased, and at the same time the whole acinus and its individual cells are considerably smaller. It is held that the outer stainable zone contains protoplasm, while the inner non-stainable zone contains the protoplasm-product about to be secreted, and some authorities moreover hold that the visible granules of this zone are the actual 'zymogen' or precursor of ferment, which in the act of secretion becomes ferment.

The microscopical changes above described demonstrate the discharge of material which certainly occurs in secretion; and according to Heidenhain, they are considered to be demonstrative of a double process—(a) discharge of protoplasm-product as shown by diminution of the granular unstainable zone, and (b) renewal of protoplasm as shown by increase of the homogeneous stainable zone. It has been found possible to actually observe during life changes taking place in the pancreas which are absolutely demonstrative of the discharge of visible material from secreting cells.

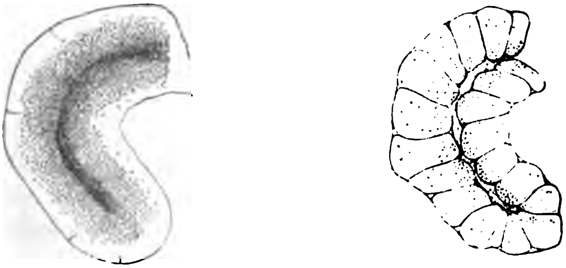


RESTING
Outer stainable zone (=*protoplasm*)
Inner stainable zone (=*protoplasm-product*, "*zymogen*")

AFTER ACTION
Increase of outer zone
Decrease of inner zone

FIG. 68.—SEROUS GLAND. DOG'S PANCREAS; ALCOHOL-CARMINE. (Heidenhain.)

In the rabbit, the pancreas is scattered between the layers of the mesentery, so that individual lobules may be examined by high powers of the microscope. Examined thus, a lobule is seen to be composed of a narrow outer zone which is homogeneous, and of a broader central zone which is granular; Kühne and Lea succeeded in observing that, with the process of secretion, the lobule gradually clears up, the nuclei and borders of individual cells become distinguishable, the granular zone becomes narrower as the homogeneous zone becomes broader, as if a tide of granular material were set up towards and into the lumen of the lobule.



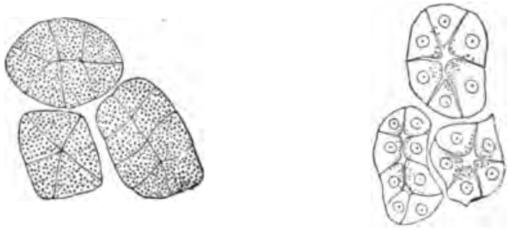
RESTING
Outer clear zone (*protoplasm*)
Inner granular zone (*zymogen*)

ACTIVE
Increase of outer zone
Decrease of inner zone (discharge of zymogen)

FIG. 69.—SEROUS GLAND. RABBIT'S PANCREAS OBSERVED DURING LIFE. (Kühne and S. Lea.)

Similar, if somewhat less distinct, changes have been observed on other serous glands. Alcohol-carmine preparations of the rabbit's parotid show that in the gland which has been caused to secrete by excitation of the sympathetic, the alveoli and individual cells are smaller and more stainable, and the cell-nuclei, which in the resting gland are more scattered and irregular in outline, are now of circular outline exhibiting a clearer structure with more distinct nucleoli. Heidenhain has moreover made out on the parotid of the dog, that similar changes of structure are effected by stimulation of the sympathetic, although no actual secretion is discharged from a cannula in the duct.

Observations on the parotid gland during actual secretion are very difficult; the best that can be done is to examine teased preparations just excised from living glands at rest or after action. This has been done by Langley, who, from a succession of preparations, has made out that clearing of the alveoli and discharge of granules takes place in this case as in that of the pancreas. It may be remarked as a difference of detail, however, that during rest no distinction of zones exists as in the case of the pancreas, but that the whole area of a lobule is granular; zones—viz. an outer clear and inner granular—appear only after secretion has made some progress.



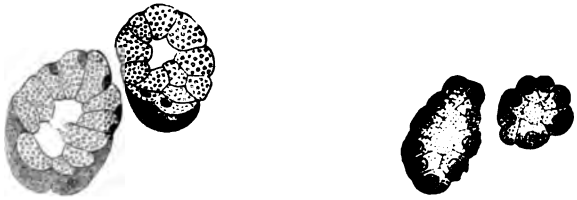
RESTING.
Uniform granular cells

AFTER ACTION.
Outer clear zone
Inner granular zone
(discharge of zymogen)

FIG. 70.—SEROUS GLAND. PAROTID; TEASED PREPARATION. (Langley.)

Turning to mucous glands, we find essentially similar changes taking place as the consequence of secretory activity, with certain differences of detail. These changes are best studied in stained sections of alcohol-hardened glands, *e.g.* of the supraorbital and submaxillary glands of the dog. In the alveoli of a resting gland so prepared two kinds of cells are seen, viz. fully-grown large mucous cells and crescentic clumps of as yet undeveloped cells.

The large mucous cells are distended with mucin, which does not stain, and which forms a broad internal zone nearest to the lumen; the outer portion of these large cells nearest to the basement membrane, is the stainable protoplasmic zone analogous with that which we have just recognised in the case of serous glands. The crescentic masses are also composed of protoplasm, and stain even better than the protoplasm of the full-grown cells. The appearance of an alveolus of a gland which has been in active and prolonged secretion presents a marked contrast; it is shrunken and as a whole much more deeply stained, so much so that a 'loaded' and a 'discharged' section can be at once distinguished by the naked eye; the large mucous cells have disappeared, so have the crescentic masses, the cells which line an acinus are of one uniform kind, stainable, and therefore to be considered as protoplasmic throughout, of moderate size, with central rounded nuclei. In a less extreme case the crescentic masses may be enlarged with increased number of nuclei—an indication of cell multiplication. These appearances are taken to be evidence of (a) destruction of adult mucous cells, together with (b) growth and development of new cells derived from the crescents. According to Langley's recent observations, the distinction between an inner granular and an outer clear zone can be made out on freshly-teased mucous gland, though less sharply than on serous gland; the granules (presumably of mucigen) are highly hygroscopic, and, unless fixed by strong alcohol or by osmic acid vapour, soon swell up and are transformed into the clear mucous material characteristic of the cells as ordinarily seen in sections.



RESTING.
Stainable demilunes (=*young protoplasmic cells*)
Unstainable mucous cells (=*adult cells*)

AFTER ACTION.
Increase of demilune cells.
Destruction of mucous cells.

FIG. 71.—MUCOUS GLAND. DOG'S SUPRA-ORBITAL; ALCOHOL-CARMINE PREPARATION. (Heidenhain and Lavdovsky.)

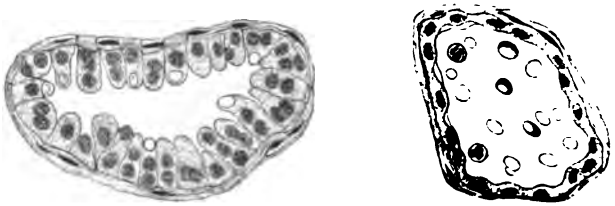
Comparing the process as it is believed to occur in serous and in mucous glands respectively, we find that in the *serous* gland there is no obvious destruction of particular cells, but a transformation of material in three stages:

1. The formation of protoplasm from blood—*outer zone.*
2. The formation of protoplasm-product (zymogen, albumin) from protoplasm—*inner zone.*
3. The formation of ferment from zymogen.

In this transmigration of matter the basement membrane is the receiving surface, the free surface of the secreting cell is the discharging surface.

In the mucous gland we recognise the same three changes. 1. The formation of protoplasm from blood (crescentic clumps of protoplasmic cells); 2. The formation of protoplasm-product from protoplasm (swollen mucous cells); 3. The formation of mucus (in the secretion) from mucigen (in the secreting cell). But in the case of the mucous cells the transmigration of matter is attended with destruction of adult cells at the discharging surface, birth and growth of new cells at the receiving surface.

The *secretion of milk* by the mammary gland closely resembles that of saliva by a mucous salivary gland; the mammary discharge is, however, a more irregular process, which establishes itself only with parturition, and which involves a far more copious secretion of organic matter than any other secretion. A healthy wet nurse yields about 1 litre of milk per diem, containing upwards of 100 grammes of solids. In correspondence with this great amount, the changes in the gland are proportionately active, the epithelial cells lining the acini breaking down rapidly, and equally rapidly growing up. In the dormant gland of the non-pregnant female the acini are almost blocked by small granular cells; in the active gland the appearances vary according as the gland or portion of gland is full or recently emptied by suckling; in the



FULL
Cylindrical, fatty, and disintegrating cells

RECENTLY EMPTIED
Flat polygonal cells

FIG. 72.—MAMMARY GLAND OF BITCH DURING LACTATION. (Heidenhain.)

full state the lining cells are swollen and protruded, and droplets of fat are a prominent feature in the cells, which have a ragged appearance, as if breaking down as well as discharging fluid secretion; in the empty state the lining cells are flattened or more or less cubical cells. In the change from the dormant to the active condition of the gland, the gland-cells which filled the alveoli undergo rapid increase and disintegration, giving rise in all probability to the colostrum corpuscles which are a characteristic feature of milk during the first days of lactation. This early milk, or 'colostrum,' contains accordingly a high percentage of proteid, and, unlike ordinary milk, coagulates on boiling.

Other physical changes associated with salivary secretion.—The act of secretion is attended with, 1. increased blood-supply; 2. expenditure of gland-substance, to which are to be added; 3. evolution of heat; 4. increased production of CO_2; and 5. electromotive changes.

The evolution of heat has been ascertained by comparing the temperature of arterial blood (in the carotid) with that of venous blood, and of saliva, the observations having been taken on the dog's submaxillary. During repose of the gland there is no constant difference of temperature between the various fluids named, but when the gland is in action, the temperature of venous blood and of saliva is higher (as much as 1·5°) than that of arterial blood, *i.e.* the active gland is a source of heat (Ludwig.)

We have seen that the percentage of CO_2 is smaller in the venous blood of active than in that of resting gland; an increased production of CO_2 in an active gland is only to be recognised by taking into account the great amount of blood flowing through an active gland, *i.e.* about fourfold that flowing through a resting gland. Calculations so made of the absolute amount of CO_2 produced, show that it is greater during activity than during repose, although the percentage of CO_2 in the blood is lower.

The electromotive changes will be considered in Chapter XI.

Influence of the nervous system.—The effect of nerves upon salivary secretion is of great importance, inasmuch as it has furnished the foundation of all definite knowledge relating to the nervous mechanism of secretion.

The chief facts were ascertained by experiments on the submaxillary gland of the dog, and have been confirmed by experiments on the same gland of other animals as well as upon the parotid gland.

The submaxillary gland of the dog is innervated through two channels, viz. the chorda tympani and the cervical sympathetic.

We have already learned that, as regards action upon the vessels, the chorda tympani dilates, and the sympathetic constricts them, the nerves thereby exercising an indirect influence upon the secreting cells. We have now to learn that both these nerves also act directly upon the secreting cell. Proofs of this:—

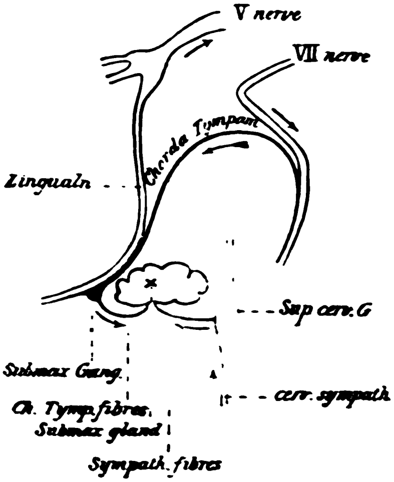


FIG. 73.

Diagram to illustrate the nervous channels to the submaxillary gland of the right side. Chorda tympani fibres pass to it through the submaxillary ganglion. Sympathetic fibres reach it by branches from the superior cervical ganglion which accompany the arteries of the gland.

1. In the first place we have to recognise that secretion is the act of the secreting cell, and not the passive filtration of fluid through its substance under the influence of blood-pressure. Ludwig showed, by means of manometers inserted in the salivary duct and in the carotid artery, that salivary pressure in the duct may reach double the amount of the arterial pressure in the carotid. The greater pressure cannot be derived from the lesser, *i.e.* secretory pressure cannot be derived from arterial pressure, but must take origin from the secreting cell. This fundamental point is confirmed by other, if less cogent, experiments.

2. Immediately after death, even on a head separated from the body, a little salivary secretion can be brought on by exciting the chorda tympani. The observation is however less convincing in the fact than in the account of the fact—only a drop or two of saliva can be thus obtained, and room is left to imagine that this minute amount is squeezed out rather than secreted.

The *post-mortem* proof of direct secreto-motor nerves is more satisfactory in the case of the sweat-glands; stimulation of the peripheral end of a kitten's sciatic will cause beads of sweat to appear on the pad for as long as half an hour after death, or even after amputation of the limb.

3. A dog is poisoned by a suitable dose of atropin, *i.e.* one sufficient to arrest secretion; the peripheral end of the chorda tympani is stimulated, the vessels dilate, but no secretion ensues. This experiment proves that secretion is not the necessary physical consequence of increased blood-supply, since the latter can be obtained without the former.

Accepting as proved the direct action upon the secreting cell of secreto-motor nerves, we must still bear in mind that there is normally an association of vaso-dilatation with increased secretion and of vaso-constriction with diminished secretion. There can be no doubt that increased blood-flow increases secretion, and that diminished blood-flow diminishes secretion. Normal variations of function never occur otherwise; for instance, when a horse begins to eat, saliva flows copiously, and the blood-flow through the active gland is fourfold that which takes place through the resting gland. Can the effect of circulation upon secretion be proved? Increased secretion due to increased blood-flow is not in the case of the submaxillary gland definitely ascertained, because the means taken to increase the blood-flow (stimulation of the chorda) at the same time directly increases the secretion. But the opposite relation is definitely ascertained, viz. diminished secretion due to diminished blood-flow. If during excitation of the chorda tympani with consequently dilated vessels and copious salivation, the sympathetic be strongly stimulated, the vessels contract and the flow of saliva is arrested; the sympathetic as we shall see is secreto-motor, not secreto-inhibitory; the arrested flow of saliva must therefore be the consequence of arrested blood-flow.

We have no difficulty in admitting the conclusive character of the experiments establishing the secreto-motor action of the chorda tympani; but in consequence of the above-mentioned vascular phenomena, the proof is less clear for the sympathetic. Yet attentively regarded the proof is conclusive enough:—

1. We have seen that changes of structure signifying glandular activity are produced by excitation of the sympathetic, even when no flow of secretion manifests itself (p. 172). In other words, the sympathetic does not arrest glandular action, but excites it.

2. By properly graduated stimulation, a flow of saliva can be produced, (a) by excitation of the chorda tympani alone, (b) by excitation of the chorda tympani and sympathetic simultaneously. In the first case, the saliva is watery, containing very little

organic matter; in the second case, it is much thicker, and contains a much larger amount of organic matter. In other words, excitation of the sympathetic, so far from counteracting excitation of the chorda, has supplemented it, and to the water has added organic matter.

3. By a variation of the preceding experiment, the possible interference of vaso-constriction is avoided. The chorda tympani is stimulated (a) before, and (b) after, a period of sympathetic stimulation. The saliva secreted during the first period is thin, that secreted during the second period is comparatively thick, *i.e.* the sympathetic excitation has added organic matter to the water.

4. Atropin administered in such dose as to abolish the effect of chorda excitation, leaves the sympathetic excitability intact, and excitation of the sympathetic now produces a scanty thick secretion.

The general conclusion which has been drawn is that both nerves are secreto-motor, that the chorda tympani contains a predominance of fibres provoking discharge of water, while the sympathetic contains a predominance of fibres provoking the formation and discharge of organic matter; to this last kind of fibres the term 'trophic' has been applied, but they are more correctly speaking katatrophic or katabolic. In summary we have then *The chorda tympani is vaso-dilatator and secreto-motor of water. The sympathetic is vaso-constrictor and secreto-motor of organic matter.*

Similar experiments have led to similar conclusions with reference to the parotid gland, although, owing to anatomical conditions, this gland has been less frequently studied. The sympathetic is the vaso-constrictor and secreto-motor ('trophic') nerve; the nerve of Jacobson is the cerebral or vaso-dilatator and secreto-motor (water) nerve.

Reflex salivary secretion.—The effects just described are those obtained by the experimental stimulation of efferent nerves. The natural secretion of saliva is a reflex act involving afferent nerves, nerve centre, and efferent nerves, the nerve-centre being situated in the spinal bulb, and the afferent channels being the nerves of taste more particularly, but also other nerves, namely, those from the nose, and eye, and ear, and stomach. A reflex flow of saliva may be caused through the nerves of taste, by a 'tasty' morsel in the mouth, or through the nerve of common-sensation by the mechanical excitation of a bit of india-rubber, or by the irritation of sore gums, or of a bad tooth ; it may be caused through the nerves of smell or of sight, by the odour or by the appearance of savoury food ; it may be provoked by material in the stomach, or by a gravid uterus ; it may be provoked or suspended by any passing thought or emotion ; fear dries the mouth ; the mere thought of saliva calls forth saliva in abundance.

The submaxillary ganglion.—It was at one time supposed that the submaxillary ganglion was capable of acting as a peripheral centre in a kind of reflex secretion of saliva. The supposition has however been disproved.

Particular kinds of saliva.—We have seen that there are several kinds of saliva—submaxillary, parotid, sublingual—according to the gland from which it comes ; mucous and serous, according as a gland secretes mucin or albumin with the water which all the glands secrete. The separate salivæ are obtained by catheterisation of the several ducts, *i.e.* by inserting a cannula into Stenson's duct to obtain parotid saliva, into Wharton's duct to obtain submaxillary saliva, into the ducts of Rivinus to obtain sublingual saliva.

From an experimental point of view, two different kinds of saliva have been distinguished, more particularly in the case of the dog's submaxillary, according as the secretion has taken place during excitation of the sympathetic or of the cerebral nerve (chorda tympani). The first is spoken of as *sympathetic saliva*, and is extremely thick, viscid, and rich in organic matter, and scanty in quantity as compared with the second, which is termed *chorda* or *cerebral saliva*, and is far more abundant and watery—in short the former is a concentrated, and the latter a dilute secretion. This difference between sympathetic and chorda saliva is not, however, of a constant character ; thus from the submaxillary of the dog and of the rabbit, sympathetic saliva is thick, chorda saliva is watery, but on the cat both are watery, and the difference, if any, is the other way, sympathetic saliva being usually the more dilute. In relation with nervous action a third kind of saliva remains to be mentioned, viz. *paralytic saliva*, which is extremely watery and copious ; it comes on a few hours after section of the chorda tympani, and in the course of a few days the paralysed gland is distinctly smaller and lighter than the gland of the opposite side ; at the end of a month or six weeks the weight of the atrophied gland may have fallen ½ to ⅔ that of the normal gland. The histological characters are (according to Langley) those of resting gland. It is to be remarked that these effects (paralytic secretion and gland atrophy) are due to section of the cerebral nerve alone, and that they do not ensue upon division of the sympathetic nerve (the so-called 'trophic' nerve) nor upon extirpation of the superior cervical ganglion.

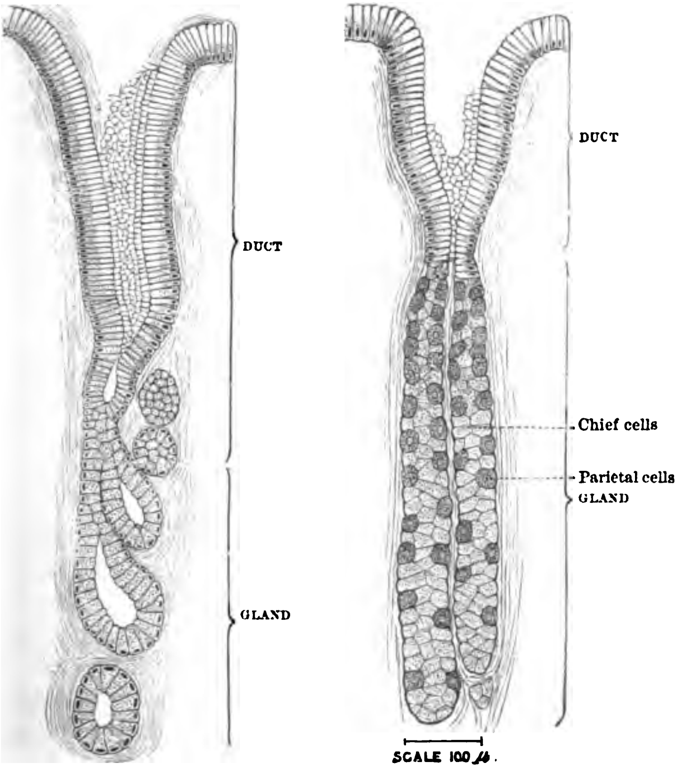
Effect of drugs.—The two drugs which have been most fully studied as regards their effect on salivary secretion are *atropin* and *pilocarpin.* Attention has also been given to the action of physostigmin, of nicotin, and of muscarin. Atropin—as small a dose as 1 milligramme on man—makes the mouth dry. On the dog, according to Heidenhain, 10 to 15 milligrammes arrest the secreto-motor action of the chorda tympani, without interfering with its vaso-dilating action, or with either the vaso-constrictor or the secreto-motor action of the sympathetic, and the dose was increased to as much as 100 mg. without implicating the sympathetic. Atropin is therefore regarded as producing an interruption of function at the junction between chorda nerve-fibre, and submaxillary secreting cell. On the cat this difference, as Langley has shown, does not hold good; in this case both sympathetic and chorda saliva are watery, and atropin (at a somewhat higher dose, it is true) abolishes the secretory effect of sympathetic as well as of chorda stimulation.

The paralysing effect of atropin is counteracted by pilocarpin; and *vice versâ* the exciting effect of pilocarpin is counteracted by atropin. Pilocarpin in very small amount (1 to 5 milligrammes on the cat) causes a copious flow of saliva, but in large doses (100 to 200 mg.) arrests it and paralyses the secretory nerves. The antagonism between atropin and pilocarpin thus holds good only for small doses. The exciting action of pilocarpin is in part central, in part peripheral; it is partly central, since section of the chorda tympani diminishes the exaggerated secretion; it is partly peripheral, since the secretion continues excessive after both the secreto-motor nerves have been divided. *Muscarin*, *nicotin*, and *physostigmin* are very similar in their action to pilocarpin; in small doses they excite, in large doses they abolish, salivary secretion; and as in the case of pilocarpin, the exaggeration of secretion produced by small doses is suppressed by atropin.

II. Gastric Juice

Physiological anatomy of the stomach.—The stomach is a secreting churn—secreting by virtue of the glands of its mucous membrane, a churn by virtue of its layers of muscle.

The mucous membrane of the stomach differs in structure in the cardiac and pyloric portions of the viscus. The glands of the cardiac end are comparatively long-branched tubules opening on the surface by a short neck or duct; those of the pyloric end are comparatively short-branched tubules opening on the surface by a long neck or duct. In both kinds of gland the neck is lined with columnar epithelium like that lining the free surface of the mucosa; the gland proper is in the pyloric region lined by



PYLORIC CARDIAC

FIG. 74.—GASTRIC GLANDS. (From Heidenhain after Ebstein)

granular cubical cells, in the cardiac region by similar granular cubical cells (chief cells) and by ovoid parietal cells (accessory cells). We shall see grounds for admitting that these two kinds of cells contribute different constituents to the gastric secretion, the chief cells being the source of pepsin, the accessory cells being the source of acid.

The changes consequent upon secretory activity, which are a prominent and well-known event in the salivary glands, have also been studied in the gastric glands, and very similar though not identical changes have been observed. Heidenhain describes the changes occurring in the dog's stomach after food as follows:—During the first six hours, the chief cells are enlarged, clouded and more stainable, the ovoid cells are somewhat swollen. From the 6th to the 9th hour, the chief cells shrink more and more, and become more cloudy, the ovoid cells are still swollen. This state lasts till the 13th to 15th hour. From the 15th to 20th hour, the chief cells gradually enlarge again and clear up, the ovoid cells shrink; the gland thus resumes its normal appearance during fasting. This account applies to the cardiac end of the stomach; in the glands of the pyloric end containing only chief cells, the changes occur somewhat later; it should be added that the times given above are liable to great fluctuation.

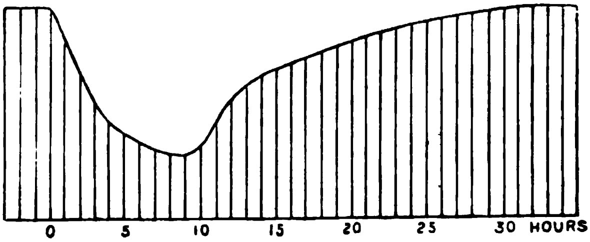


FIG. 75.

Peptic activity of gastric mucous membrane (cardiac) after the ingestion of food. (Grützner.)

Comparing the appearances of the chief cells with the peptic power of the mucous membrane at various periods after a meal, it is found that with the large clear relatively unstainable cell, the digestive power of a given weight of mucous membrane is three times as great as when the chief cells are in the shrunken, clouded, and more stainable state. Heidenhain deduces from these observations conclusions essentially identical with those previously given in the case of salivary glands. During the fasting state, the protoplasm-product zymogen (in this case pepsinogen), is formed from protoplasm and stored in the chief cells. During secretion three processes are simultaneously progressing:—(1) The new growth of protoplasm. (2) Continued production of pepsinogen. (3) Discharge of pepsinogen as pepsin.

Heidenhain's observations were made on stained sections of alcohol-hardened stomachs of dogs. Langley has made similar observations on the fresh stomachs of frogs and of mammalia, and comes to a similar conclusion. In the fasting state (18 hours after a meal) he finds the glands uniformly granular throughout; as digestion proceeds he observes the formation of zones—outer clear and inner granular—and the progress of a tide of granules towards the lumen of the gland; he considers that the granules are the actual pepsinogen. Both the above accounts thus attribute the alterations entirely to the outgoing secretion, and not to any incoming absorption of food.

Gastric juice.—The secretion of the gastric glands is a colourless acid fluid, of low specific gravity (1002), containing *pepsin* and other ferments, and possessing a slight antiseptic action. The acidity of gastric juice is due to free hydrochloric acid, amounting to 2 per 1,000 of the fluid. The total daily secretion of fluid has been estimated at $\frac{1}{10}$ the body-weight, or 7 litres; it must not, however, be supposed that this is discharged from the body; it is reabsorbed in the small intestine. The principal ferment—pepsin—acting in concert with hydrochloric acid, converts proteids into peptones. Another ferment, the rennet ferment, brings about the curdling of milk.

Nature of the gastric acid.—It was formerly a much-debated question whether hydrochloric or lactic acid is the normal acid of gastric juice; now, however, it is accepted to be the former, for these among other reasons: 1. Separate estimates (*a*) of the chlorine, (*b*) of the bases present in gastric juice, show that the amount of chlorine present is in excess of the amount which could be combined with the amount of basic elements; such excess can be present only in one form, viz. as hydrochloric acid; 2. Several of the aniline dyes, such as methyl violet, are altered in colour far more readily by mineral than by organic acids; gastric juice is found to act like a mineral acid in this respect; 3. A mineral acid (*e.g.* hydrochloric acid) is very soluble in water, hardly at all soluble in ether; an organic acid (*e.g.* lactic acid) is soluble in water and in ether. If fresh gastric juice is shaken up with ether the latter is subsequently found to contain hardly any acid, from which the conclusion is drawn that the acid in gastric juice is not an organic, but a mineral acid; 4. Uffelmann's test for lactic acid gives a negative result with fresh gastric juice. The test-reagent consists in a 1 per cent. solution of carbolic acid *plus* 3 drops of liq. ferri perchloridi to the 100 c.c.; this solution is blue and changes to yellow by lactic acid, while it is not affected by hydrochloric acid.

Action of gastric juice.—The action of gastric juice has been studied by observing the changes which swallowed food undergoes in the stomach, or by following the transformation of foodstuffs which is effected by gastric juice out of the body. For the latter purpose we may use natural gastric juice obtained from a fistula, or artificial gastric juice made by extracting the mucous membrane of a recently killed animal with dilute hydrochloric acid (1 per 1,000) or with glycerine. The action of gastric juice bears exclusively on proteids, which are dissolved and converted into peptones. If we examined (*a*) the contents of the stomach during the digestion of proteid, (*b*) the blood of the portal vein, we should find in the portal blood no trace of peptone, in the contents of the stomach, little or none. This apparent paradox depends on these two facts: 1. that peptone is absorbed as fast as it is formed; 2. that it is reconverted into serum-albumin as fast as it is absorbed. Otherwise expressed, albumin traverses the mucous membrane temporarily disguised as peptone; it is albumin before passage, albumin after passage, peptone only during passage.

All descriptions of the successive changes which a proteid undergoes when acted upon by pepsin, are based upon prolonged artificial digestions made '*in vitro*.' Without entering upon a critical account and comparison with each other of the different views of the process which have been advanced, we shall in this place confine our attention to the easily verifiable results of one representative experiment. A handful of boiled fibrin is allowed to digest in a warm chamber at 35° to 40° in a litre of dilute hydrochloric acid, strength 1·5 per 1,000, to which has been added a small quantity of 'gastric glycerine' (*i.e.* a glycerine extract of the mucous membrane of dog's or pig's stomach). We have thus all the conditions necessary to the accomplishment of an artificial digestion, viz. fibrin as the proteid to be digested, an optimum temperature, a dilute acid, and ferment (pepsin) in the gastric glycerine. A few hours later, less or more, in proportion with the power of the glycerine extract employed, we shall by appropriate tests find in solution at least three forms of proteid. (1.) By carefully neutralising a portion of the fluid with sodium carbonate, a precipitate will be obtained. This neutralisation precipitate is *acid-albumin*, otherwise called *syntonin.* (2.) On adding strong HNO_3 to another portion of the fluid, a precipitate is obtained, which disappears on heating and returns on cooling. This precipitate is *albumose*, sometimes called *propeptone*, or more generally *proteose.* (3.) A third portion of the fluid is shaken with excess of ammonium sulphate (by which all proteids except peptone are precipitated). The fluid is filtered and to it are added a trace of copper sulphate and an excess of sodium hydrate; a rose-colour appears which indicates the presence of *peptone.*

We have learned from this experiment, firstly, the conditions necessary to artificial digestion; secondly, the changes which a solid proteid undergoes in the process. If any one of the conditions be unfulfilled, digestion does not take place; if the experiment be repeated, omitting the acid, or omitting the ferment, or keeping the mixture cold without omitting any ingredient, digestion does not take place. Or if it be repeated with ferment which has been boiled, the same negative result occurs, this indeed being the fundamental test informing us that a ferment is concerned in the change.

As regards the phases of the transformation, we learn that proteid is first dissolved, becoming acid-albumin or syntonin, and that passing through a preliminary stage (propeptone or albumose) it finally becomes peptone. The sequence reminds us of the starch-to-sugar change effected by ptyalin; dextrin is the name of the intermediate station between starch and sugar, albumose is the name of the intermediate station between proteid and peptone; and as there are grounds for admitting that the intermediate between starch and sugar is a series of dextrins, rather than one definite dextrin, so there are reasons for presuming that the intermediate between proteid and peptone is a series of albumoses, rather than one definite albumose. The analogy is drawn still closer when we recognise that the final product of a gastric digest is composed of albumose and peptone, as the final product of a salivary digest is composed of dextrin and sugar.

Brücke, Meissner, and Kühne.—The account contained in the above description is not so different as might at first sight appear from the accounts which have been given by Brücke, by Meissner, and by Kühne. All agree in the fundamental point, that between the initial proteid and the resultant proteid there are intermediate products; the chief point of divergence between them is as regards the naming and identification of these intermediate products. According to Brücke's nomenclature the sequence is:—

1. Proteid. 2. Parapeptone. 3. Peptone.

According to Meissner's nomenclature it is:—

1. Proteid. 2. Syntonin. 3. Parapeptone and Peptone.

According to Kühne's nomenclature it is:—

1. Proteid. 2. Albumose. 3. Peptone, with a cleavage of the proteid molecule into two moieties.

According to the nomenclature adopted above the sequence is:—

1. Proteid. 2. Acid-albumin. 3. Albumose. 4. Albumose and Peptone

The apparent differences between these various accounts are muc reduced when we recognise that 'acid-albumin,' 'syntonin' (Meissner) 'parapeptone' (Brücke), are synonymous terms for one and the sam substance. The chief real differences are that Meissner considered th process to be an incomplete one, and used the term 'parapeptone' t denote the incomplete peptone found in the product of an artificia digestion, while Kühne considers that the proteid molecule splits int two in the process, giving rise to two parallel series of bodies, one comparatively stable, distinguished by the prefix '*anti-*,' the other les stable, distinguished by the prefix '*hemi-*;' these are anti-albumos and hemi-albumose in the intermediate stage, anti-peptone and hemi peptone in the final stage. Kühne's anti-albumose is probably th same body as Meissner's para-peptone; it is the more stable substance, difficult to transform into peptone, and when so transforme (anti-peptone) not capable of further change under the influence of pancreatic juice. Kühne's hemi-albumose is probably the same body a that which Meissner described under the name of 'a peptone;' it is th less stable substance, easily transformed into a peptone (hemi-peptone which if submitted to pancreatic digestion becomes decomposed in leucin, tyrosin, and ammonia.

Some of the obscurity in which the subject of proteid digestion ha been enveloped is due to the indefinite use of the term 'peptone Formerly it included substances which are now called 'albumose; old-style peptone is a mixture of albumose and peptone, which when i solution can be separated by saturation with ammonium sulphat albumose being precipitated thereby, while peptone remains in solutio Peptone, as the term is now used, is restricted to that substance substances which remain in solution after saturation with ammonium sulphate. Commercial peptone contains a large quantity of albumose, but very little true 'peptone.'

Pepsin.—We have learned that a ferment—pepsin—is *the* essential constituent of gastric juice. What are the source, properties, and methods of estimation of this important agent? As regards its *source*, it is formed by the chief cells of the cardiac and of the pyloric glands. The nature of the evidence upon which this statement rests is as follows:—The cardiac glands contain two kinds of cells—the chief cells and the accessory cells; the pyloric glands contain only one kind of cells—the chief cells. The secretion of the cardiac end of the stomach contains pepsin and acid; the secretion of the pyloric end of the stomach contains only pepsin. Combining these data, it follows that the chief cells contribute pepsin, while the accessory cells contribute acid to the complete secretion.

In the account given above of the alterations of structure coincident with secretory activity, it was stated that in the cells a granular substance is present which is not pepsin but *pepsinogen.* The evidence upon which this statement rests is the following:—A fresh mucous membrane is extracted with glycerine, and the extract is found to have a very slight activity; another portion of the same mucous membrane previously submitted to the action of HCl (·15 per cent.) yields a glycerine extract of considerable activity. The difference is attributable to a formation of pepsin from pepsinogen under the influence of weak acid.

Estimation of pepsin.—Pepsin, like other ferments, has never been completely isolated, but has only been obtained in solution. Like other ferments it has indefinite power; presumably minute quantities effect the transformation of a large bulk of proteid, provided that the resultant peptone is not suffered to accumulate; a single dog's stomach treated with 200 litres of acidulated water digested 75 kilos of albumen in fifteen days. The quantity of pepsin in a mucous membrane cannot be directly measured, but only indirectly estimated by comparing with some arbitrary standard the activity of a given weight of mucous membrane. For this purpose *Grützner's method* is the most serviceable. It is as follows:—Boiled fibrin is stained with an ammoniacal solution of carmine (·2 per cent.) and well washed, first with water, then with dilute HCl (·1 per cent.), until the washings are completely colourless. A portion of this fibrin acted upon by a gastric extract will be dissolved, the carmine belonging to the dissolved fibrin will be set free in the fluid, and tinge it more or less deeply in proportion with the amount of fibrin dissolved. The depth of tint is estimated by comparing it with that of a series of ten test tubes, I to X, containing

I	II	III	IV	V	VI	VII	VIII	IX	X
19·9	19·8	19·7	19·6	19·5	19·4	19·3	19·2	19·1	19·0.....c.c. water.
·1	·2	·3	·4	·5	·6	·7	·8	·9	1·0.....c.c. ·1% carmine-glycerine,

forming thus a colour scale. If, for instance, we have to compare the digestive activity of two fluids, we may leave, say, 20 c.c. of each acidified with HCl to the proper degree in a warm chamber with 1 c.c. of carmine fibrin. If at the end of a given period the tints of the two solutions are judged to correspond with III. and with VI. of the colour scale, we conclude that the second solution is twice as active as the first, and presume tha it contains twice as much pepsin. Judgment must of cours be exercised in the use of the method, and the conditions o observation so adjusted that convenient tints within the scal may be produced in a given time.

The relative amounts of free pepsin and of fixed pepsinoge present in a mucous membrane cannot be precisely determined but only roughly estimated by comparing the digestive powe of simple glycerine extract with that of the subsequent acid extract and to obtain comparable values it is necessary to adopt regula periods of extraction; *e.g.* to admit for the pepsin extract th product of eight days' extraction of a given weight of dried an pulverised mucosa with one hundred times its weight of gly cerine—for the pepsinogen proportion the product of one day' extraction of the residue with 1,000 times its weight of dilute HC (0·15 per cent.). The relative activities of the two extracts ca then be compared by Grützner's method as just described.

Langley estimates the relative amounts of pepsin and pepsi ogen present in a gastric extract by comparing its activit before and after it has been submitted to the action of an equa bulk of Na_2CO_3 (1 per cent.) for 15 to 30 seconds. If f instance the peptic activity of an extract is equal to X befo Na_2CO_3 and to V after Na_2Co_3 he concludes that the solution co tains equal amounts of pepsin and pepsinogen. If it is X befor Na_2CO_3 and II after Na_2CO_3, the proportion of pepsin to pepsi ogen would be $\frac{8}{2}$ or 4 to 1. If it is X before Na_2CO_3 and VIII aft Na_2CO_3 the proportion of pepsin to pepsinogen would be $\frac{2}{8}$ or 1 to

It is to be observed that the division made on either of these two methods is a conventional one; in the first method we agree to call what is in the glycerin extract 'pepsin,' what is in the subsequent acid extract 'pepsinogen;' in the second method we agree to attribute the loss of digestive power in consequence of the action of an equal volume of Na_2CO_3 during 30 seconds to 'pepsin,' and the digestive power remaining after such action to 'pepsinogen.'

Other ferments.—It has long been known that the fourth stomach of the calf causes a rapid coagulation of milk; under the name of rennet an extract of calf's stomach is commonly employed to make 'curds and whey' in the process of cheese manufacture. Hammarsten has shown that in addition to pepsin, gastric juice (especially that of sucking animals) contains a distinct rennet ferment. It has the property of curdling milk with alkaline reaction, like other ferments is destroyed by boiling, and its essential effect is the production of a clotted body, *casein*, from a precursor existing in solution in milk, '*caseinogen*;' the production of fibrin from fibrinogen by ferment action has already been alluded to as a similar event (p. 35), and we shall meet with a third similar instance in the case of myosin (p. 321). Alkalinity during the process of curdling is the main point in the rennet action; acid can of itself curdle milk, no ferment action being involved, so that curdling in an acid medium is not demonstrative of the presence of a ferment.

Evidence of the presence of a lactic acid ferment (producing lactic acid from lactose), of a glucose ferment (converting saccharose to glucose), of a fat-splitting ferment (producing fatty acid from fat), has moreover been obtained by various observers. But the effects of these are hardly deserving of mention, as they are not characteristic of gastric juice nor significant of its normal action. It is of more practical importance to recognise that gastric juice is antiseptic; left to itself it resists putrefaction for an indefinite period, and normally it no doubt has a 'sterilising' action upon swallowed materials.

Influence of the nervous system.—There is no direct proof of the existence of any regulation of gastric secretion by secreto-motor nerves; neither section nor excitation of the sympathetic or of the pneumogastric nerves produces any alteration of gastric secretion; yet certain facts suggest the possibility that nerves may take part in the regulation of secretion. The flow of gastric juice is not continuous, but a responsive outflow consequent upon the ingestion of food. No doubt the direct mechanical action o swallowed food may excite secretion from the mucous membrane, but this is not all; secretion has been observed to occu when, owing to stricture of the gullet, no food could reach the stomach. Mechanical excitation of the mucous membran has been seen to produce secretion of gastric juice—this is a direc action independent of nerves. Chemical excitation likewis exercises a direct action on the mucous membrane—a perfectl indigestible body such as glass or india-rubber by its mechanica action produces secretion; but a digestible body such as a bi of meat produces a far more active secretion, and Schiff ha shown that dextrin and meat extract are particularly active i causing a true peptic secretion from a previously exhauste stomach; alkalies also are powerful excitants of the secretion and one of the services of saliva is thus to promote the flow o gastric juice. But those various facts contain no *proof* of a action of the nervous system, the effects can be referred to chemical action of substances absorbed into and carried by th blood, when they are not attributable to direct mechanical o chemical excitation.

A *gastric fistula* is a permanent abnormal opening leading through the abdominal wall into the stomach. Such a opening may be effected by accident or by surgical operatio and can then be utilised for th study of gastric digestion. *gastric cæcum* is a blind pock formed by operation and compos of a portion of the stomach. Th principle of the operation is follows. A portion of the stomac *a*, *b*, *c*, *d*, is included between tw incisions *a b* and *c d*. The tw edges *a b* and *c d* are sewn t gether and soon heal, so that t continuity of the viscus is restore One of the two edges of the shad portion *a b c d*, which is to form the cæcum, is sewn up a allowed to heal so as to form the bottom of the pocket. T other edge is also sewn up with the exception of a small orifi the borders of which are fixed to the borders of a correspondi

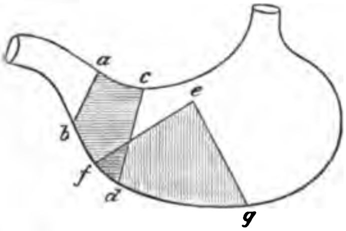


FIG. 76.

Parts of the stomach from which gastric cæca have been formed; pyloric cæcum from *a*, *b*, *c*, *d*; cardiac cæcum from *e*, *f*, *g*.—Heidenhain.

orifice left in the abdominal wall. The final result of the operation is thus an isolated pocket formed of pyloric or of cardiac stomach-wall, with an external orifice through which the mucous membrane can be observed, or materials introduced, or secretions removed. A pyloric cæcum so formed secretes a thick mucous alkaline fluid, which contains pepsin; a cardiac cæcum secretes a thin highly acid fluid which also contains pepsin. Swallowed food provokes secretion from such a cardiac cæcum, although it does not come in direct contact with it; the secretion thus excited begins in about 15 to 30 minutes, and is considered not to be a reflex effect, as it does not occur unless material is digested and absorbed by the main stomach; it seems therefore to be due to a chemical stimulation by blood which is charged with products of digestion.

Self-digestion post mortem.—Under certain circumstances the stomach can digest itself, and the question has been asked—why does it not normally do so during life? The stomach of an animal removed and left in a warm chamber in a sufficient quantity of dilute hydrochloric acid will become completely dissolved. An animal killed during digestion and examined a few hours later may be found with the stomach perforated by self-digestion, and with more or less extensive destruction of surrounding tissues. The non-digestion of the living stomach by its own gastric juice during life is generally referred to the alkalinity of the blood, but it is a sufficient answer to simply paraphrase the question and to say that living tissue resists digestive action so long as it is living.

An experiment by Bernard, which is quoted to show that living tissue can be digested, shows no such thing. The experiment consists in the introduction of the legs of a living frog into a dog's stomach through a fistula; the legs become digested, but we have good reason to say that they are first killed, then digested. Nor is the protective influence of alkaline blood a good and sufficient answer, for it does not apply to pancreatic fluid which acts on proteids in an alkaline medium, yet does not digest the living proteid with which it may come in contact.

Classification and identification of proteids.—Frequent allusion has been made to the various proteids found in the solids and fluids of the animal *body*, and the methods by which these proteids are separated and *identified* are described in their place under *blood*, *muscle, urine, &c.* It will be found convenient at this stage to mak ourselves familiar with the chief tests, by means of which proteids a a class are recognised, and with the distinguishing tests characteristi of the chief members of the class.

The chief proteids met with as such in the animal body are th *albumins* and the *globulins.* Several other bodies belonging to th proteid class, do not exist ready formed in the living body, but are pro duced in the course of death changes—*fibrin* and *myosin*; or in th process of digestion—*derived albumins, albumoses* and *peptones*; or b the manipulations used for their separation—*coagulated albumin.* I addition to these chief groups, there are numerous other bodies, whic although resembling proteids in their chemical composition, are marke out by some distinguishing characteristic, and collectively spoken under the title of *albuminoids:—mucin, elastin, chondrin, collage* *nuclein, gelatin,* and the pathological product *lardacein* belong to th group; and *hæmoglobin,* although not classed with proteids, diffe from them only by the presence of iron.

The classification of proteids is principally based upon their sol bilities in distilled water, in dilute solutions of neutral salts, and saturated saline solutions. *Albumins* are soluble in distilled water, dilute and in saturated solutions of sodium or of magnesium sulpha but insoluble in saturated solution of ammonium sulphate; they ca therefore be precipitated by saturating their solutions with the la named salt. *Globulins* are insoluble in distilled water and in saturat saline solutions, but soluble in dilute saline solutions; they can the fore be precipitated from such solutions by removal of the salt dialysis, or by saturation with a neutral salt such as magnesiu sulphate. The digestion proteids—*acid-* and *alkali-albumin, alb* *moses,* and *peptones*—are characterised by their great solubilit *peptones* are soluble in all the media named above and are not preci tated by saturation with ammonium sulphate; *albumoses* are solu in water and in dilute saline solutions, but insoluble in satura ammonium sulphate solution; they are, therefore, precipitated fr solution by saturation with this salt: *acid-albumin* and *alkali-al* *min* are soluble in dilute acid or alkaline solution, but insoluble distilled water and in dilute saline; they are therefore precipitated exact neutralisation of their solutions. The *post-mortem* proteids *fibrin* and *myosin*—are comparatively insoluble; like the globul from which they are derived, they are insoluble in distilled water, a in saturated saline solutions; they are also insoluble in dilute sal solutions, but soluble in saline solutions of moderate strength—5 to per cent. *Coagulated albumin* is insoluble in all these media; boil with a strong acid, or warming with a weak acid, *plus* a digestive ment, is required for its solution.

All proteids in solution give the following colour reactions :—

1. *The xanthoproteic reaction.*—Boiling with nitric acid turns the solution to yellow, which is deepened to orange by the subsequent addition of strong ammonia or potash.

2. *Millon's reaction.*—Boiling with Millon's reagent (mercurous and mercuric nitrates) turns the solution red.

3. *The biuret reaction.*—A trace of copper sulphate and excess of caustic soda or potash give a violet or rose colour.

The first two tests applied to concentrated solutions give a *precipitate*, turning yellow, orange, or red, as the case may be.

By means of heat coagulation a proteid is known to belong to one or other of the following groups, (*a*) to the albumins or globulins which coagulate, or (*b*) to the derived albumins, albumoses, or peptones, which are not coagulated by heat.

The proteids coagulable by heat are distinguished into albumins and globulins by saturation with magnesium sulphate; globulins are, albumins are not precipitated, and if both are present, globulins can be retained on a filter paper, while albumins pass through with the filtrate.

The two chief forms of albumin ordinarily met with are egg-albumin and serum-albumin; the first of these is, the second is not coagulated by shaking with ether. Muscle-albumin is practically indistinguishable from serum-albumin. The globulin class includes serum-globulin and fibrinogen, and is widely distributed in the solid organs, *e.g.* in muscle as muscle-globulin, in the crystalline lens as crystallin. We do not in ordinary analysis attempt to distinguish between different members of this class, although actually they have been distinguished by varying solubilities in saline solutions, and by their behaviour with fibrin-ferment. The *post-mortem* proteids—fibrin and myosin—are also included in the globulin class. They are to some extent distinguished by their solubilities in saline solutions, and by the temperature at which they coagulate.

To further distinguish between and identify the group of proteids which are not coagulable by heat, we must examine (1) the reaction, (2) the character of the biuret colour, (3) the behaviour to saturation with ammonium sulphate.

Acid-albumin in solution has an acid reaction and is precipitated by cautious neutralisation, excess of alkali being avoided.

Alkali-albumin in solution has an alkaline reaction, and is likewise precipitated by cautious neutralisation with acid.

Albumoses are precipitated by saturation with ammonium sulphate, peptones are not. If a proteid fluid which is not coagulable by heat is neutralised exactly and thrown on a filter, acid or alkali albumins are retained, albumoses and peptones pass in the filtrate; if this filtrate is saturated with ammonium sulphate and filtered, albumoses are retained and peptones pass through; the presence of peptones is recognised in this last filtrate by a rose-coloured biuret reaction, care being taken to add KHO in excess.

Summary of the Principal Proteids and of their Distinguishing Tests.

Coag. on boiling	Egg-albumin	Ether ppt.
	Serum-albumin	No ether ppt. No $MgSO_4$ ppt.
	Globulins	$MgSO_4$ ppt.
No coag. on boiling	Acid and alkali albumins	Neutralisation ppt.
	Albumoses	HNO_3 ppt. in cold, sol. by heat.
	Peptones	Pink biuret reaction in filtrate after saturation with Am_2SO_4.

Albumose.—We have already given to be understood that proteids are the most important and multiform of proximate principles, and we may take this opportunity of emphasising this point, and of indicating, as their most important member or group of members, the intermediate digestion-proteids, collectively termed albumoses. We cannot here enter upon a full account of their action upon the living body, nor shall we describe the differences provisionally accepted as characteristic of all different kinds of albumoses; but we may briefly enumerate a series of facts serving to illustrate and assert their extreme importance.

The most rapidly fatal of animal venoms, cobra-poison, owes its property to the presence of albumose. Substances produced by the proteolytic action of pathogenic microbes, and which have recently been found to promote immunity from the further action of such microbes (Wooldridge, Hankin), belong to the family of albumoses. And we may also refer back to the fact, already stated, that peptones (or, more correctly speaking, albumoses) injected into the vascular system, produce profound changes—loss of coagulability, fall of blood-pressure, and death. Enough has been said to show that proteids are also protean, and that they may offer many kinds of opportunities 'for different kinds of chemical intercourse.' One kind of proteid may be poisonous, another may be protective from further infection, and the same proteid (albumose) which nourishes the body, if it enters and is modified by the intestinal epithelium, fails to nourish a tissue with which it comes into immediate contact (see Kronecker's experiments, on p. 97), and proves actually poisonous when directly injected into the blood-vessels. For reasons of this order, and on account of the great importance which the further study of albumose is assuming, we append a summary of the principal albumoses and of the procedure by which they may be separated from each other, although it should be stated that their distinguishing properties are not such as to entitle them to be recognised as distinct bodies in the eyes of a chemist.[1]

Test	Proto-Alb.	Hetero-Alb.	Deutero-Alb.	Peptone
Biuret ($CuSO_4$, KHO)	Pink	Pink	Pink	Pink
Water, hot and cold	Soluble	Insoluble; ppt. by dialysis	Soluble	Soluble
Saturation by $NaCl$ *or* $MgSO_4$	ppt.	ppt.	no ppt. (ppt. by dilute HA)	no ppt.
Saturation by Am_2SO_4	ppt.	ppt.	ppt.	no ppt.
Nitric Acid	ppt. in cold diss. by heat returns in cold	Do.	Do. in presence of excess NaCl	no ppt.
$CuSO_4$	ppt.	ppt.	no ppt.	no ppt.

A gastric digest of fibrin, made as described on pp. 184 and 185 (after removal of heat-coagulum and neutralisation ppt. if any), contains the three albumoses and peptones; in addition to the biuret reaction, it should give the characteristic nitric acid reaction, and on dropping in distilled water a cloud should form. They may be separated as follows (Halliburton) :—

Precipitate by saturation with Am_2So_4 *and filter.*
Albumoses on filter ......Peptones in filtrate.

Dissolve in water, precipitate by saturation with NaCl and filter.
Proto- and hetero-albumose on filter ...Deutero-albumose in filtrate.

Dissolve in water, dialyse and filter. *Ppt. by alcohol, wash and dry.*
Hetero-albumose on filter ....Proto-albumose in filtrate.

Wash and dry. *Ppt. by alcohol, wash and dry.*

III. Bile and Pancreatic Juice

The Liver.—The chief functions of the liver are (1) the secretion of bile, (2) the formation of sugar. As regards its first function, the liver is an ordinary secreting gland, the duct which opens into the duodenum. As regards its second functio it is a so-called ductless gland from which elaborated produc are carried off by the outgoing venous blood; and it is a not worthy point in this respect that the liver is traversed by t main current of incoming material carried by the portal bloo These are the two chief functions of the liver, to which are to added two minor, or, at any rate, less obvious functions, vi (3) the destruction of red corpuscles, (4) the formation of ur and of other urinary substances.

---

[1] For fuller details the student should consult Halliburton's 'Chemical Physiology and Pathology,' and the papers issued from Kühne's laboratory (see Bibliography).

We shall at this stage consider only that function whereby digestive fluid is secreted, namely, the bile; the sugar functio which is subsequent to the absorption of food, will be consider under the heading 'Glycogenesis' (p. 213); the urea functio which belongs to elimination of used-up or waste proteid, w be considered at p. 244.

Physiological anatomy.—Three channels enter and leave t liver at the transverse fissure or hilum. The largest of the the *portal vein*, conveys venous blood from the digestive visce material upon which the liver exercises its elaborative actio the smallest, the *hepatic artery*, conveys arterial blood requis to the nutrition of the liver-substance; the current in these t channels is towards the liver, they penetrate into and rami in its substance and ultimately form a system of small vess between adjacent lobules, hence called *interlobular vessels*. T third channel is the *bile-duct*, in which the current of secretion from the liver, and it is noteworthy that in most animals a *g* *bladder* is present, serving as a storage chamber in which bi secreted in the intervals of digestion, is kept until requir A fourth system of vessels takes origin within the lobules, fr venules which are therefore called *intralobular*, and which conj to form the *sublobular* and the *hepatic* veins; the latter emer from the posterior border of the liver, and carries off blood u which the organ has exercised its functions.

Anatomically, as well as physiologically, each lobule is miniature liver, consisting of cells filling up the interstices tween a network of blood-capillaries and of bile-capillaries. network of blood-capillaries within a lobule is formed from interlobular or afferent vessels, and in turn forms the int lobular or efferent vessels. The lobular network of bile-capilla takes origin from the liver-cells. A noteworthy point, concern the relation of a liver-cell to the surrounding capillaries, is that blood-capillaries and bile-capillaries do not lie side by side against the cell but are separated from each other by the substance of the cell. Bile-capillaries occupy, as a rule, minute channels between the opposed surfaces of two contiguous cells; blood-capillaries occupy somewhat larger and longer channels between the adjacent edges of columns of cells. The livers of the lower animals (*e.g.* frog) are of the tubular type; sections show that its cells are arranged in double rows, belonging to a network of anastomosing tubules; and the apparently lobular type of the vertebrate liver is probably due to the vascular modification of an originally tubular structure. Physiologically regarded, each liver-cell is the functional centre; hepatic arterial blood feeds it, crude portal blood comes to it, and is modified by it, bile leaves it to do duty in the intestine, hepatic venous blood leaves it to do duty in the tissues of the body. Alterations of structure, consequent upon the absorption of food, will be considered in connection with 'glycogenesis.'

The pancreas, in its minute structure, very closely resembles a serous salivary gland, being a racemose gland with short tubular acini lined by cubical granular epithelium. It is, as has already been described (p. 171), the chosen gland in which visible tokens of secretory action have been most closely studied. The granular contents of the cells are considered to be the '*zymogen*' or protoplasm-product which is about to be transformed into ferment, and the experiments which show that the living or perfectly fresh gland contains ferment-forming or zymogenic material, and not the actual formed ferment, are, in the case of the pancreas, particularly striking and conclusive. The glycerine extract of a perfectly fresh pancreas has hardly any fermentative action; the glycerine extract of a pancreas, which has been left for twenty-four hours in the body of the animal or in a warm chamber, is powerfully active. The difference in the two cases is explained by saying that the fresh organ contains zymogen but not ferment, while in the stale organ the elaboration of ferment from zymogen has taken place. By weak acid, this conversion can be effected at once; a perfectly fresh pancreas, extracted with dilute acetic acid, yields a fluid which has fermentative power.

Bile.—*Its composition.* Bile is a reddish-brown or dirty-green fluid of slightly alkaline reaction, with a bitter taste and with a specific gravity of 1020. The daily secretion of bile is the same as that of urine, viz. about 1500 c.c. It contains:—

	Water	90 to 85 per 100
	Mucus	10 to 15 per 100
Bile-acids	Glycocholic acid	
	Taurocholic acid	
Bile-pigments	Bilirubin	
	Biliverdin	
	Cholesterin	
	Lecithin	

It does not contain any *albumin*. *Mucus*, although not properly speaking a specific constituent of bile, is generally present in such quantity that bile is the chosen fluid from which mucus is usually prepared. It gives to bile a glairy ropy consistency and is the cause of the rapid decomposition to which bile is subject, although bile itself possesses antiseptic properties by virtue of other constituents.

The specific biliary substances are the bile-pigments and the bile-acids, the acids being for the most part combined with sodium in the form of salts as glycocholate and taurocholate of soda, and forming two-thirds of the total biliary solids.

The *bile-acids*, glycocholic and taurocholic, are compounds of glycin and of taurin with cholalic acid. Glycocholic acid boiled with dilute acid or with alkali, takes up water and breaks up into glycin and cholalic acid. Taurocholic acid similarly treated breaks up into taurin and cholalic acid. Hippuric acid similarly treated breaks up into glycin and benzoic acid. Glycin is amido-acetic acid, *i.e.* a nitrogenous body; taurin is amido-isethionic acid, *i.e.* a nitrogenous body combined with a sulphur acid. Cholalic acid is a complicated non-nitrogenous body. The three reactions will be found graphically represented in the Appendix.

To separate the bile-salts from bile, the fluid evaporated to one-quarter its bulk, is made into a paste with animal charcoal, dried at 100°, then pulverised and extracted with alcohol; the bile-salts are precipitable as a crystalline mass by adding ether in excess.

To separate the two bile-acids from each other, the ether precipitate is redissolved and the solution treated with neutral lead acetate, which gives a precipitate of glycocholate of lead; the precipitate is collected on a filter, and the filtrate, treated with basic lead acetate and ammonia, gives a precipitate of taurocholate of lead which is likewise collected on a filter; to obtain the acids free of lead, the precipitates are respectively dissolved in hot alcohol, and the lead removed by a stream of H_2S; from the filtered alcoholic solutions, glycocholic and taurocholic acids are respectively precipitated by adding water. Glycocholic acid is best prepared from pig's bile, taurocholic acid from dog's bile.

The *bile-pigments*, as they normally exist in bile, are *bilirubin* and *biliverdin*—biliverdin ($C_{32}H_{36}N_4O_8$) being the more highly oxidised state of bilirubin ($C_{32}H_{36}N_4O_6$). By powerful reducing or oxidising agents less oxidised and more oxidised bodies are obtainable. Nitric acid, as employed for instance in the Gmelin test, gives as the final product a yellow substance *choletelin*, which is the most highly oxidised state of bile-pigment. On the other hand, by the reducing action of sodium amalgam, *hydrobilirubin* is produced, the least highly oxidised state of bile-pigment, and identical with the bile-pigment derivatives in urine and in fæces which are produced by the reducing action of the tissues. These relations are exhibited in the following table:—

($C_{32}H_{36}N_4O_5.2H_2O$)	*Hydrobilirubin* .	. Produced from bilirubin by the reducing action of sodium amalgam. Identical with *urobilin* and with *stercobilin*, produced by the reducing action of the tissues.
($C_{32}H_{36}N_4O_6$)	*Bilirubin* .	. Identical with *hæmatoidin*.
($C_{32}H_{36}N_4O_8$)	*Biliverdin* .	. Produced from bilirubin by oxidation.
($C_{32}H_{36}N_4O_{12}$)	*Choletelin* .	. Produced from bilirubin by the oxidising action of nitric acid.

Bilirubin can be obtained in quantity from 'red' gall-stones. These are pounded, treated with hydrochloric acid to dissolve chalk, and extracted with chloroform; the chloroform solution yields crystals of bilirubin.

Cholesterin ($C_{26}H_{44}O,H_2O$) is a monatomic alcohol crystallising in rhombic plates or needles, widely distributed in the animal and vegetable kingdoms, and probably a derivative of proteid, although itself a non-nitrogenous body. The two materials which contain it in greatest abundance are the bile and the brain. White gall-stones in particular, which are a deposit from bile, are almost entirely composed of cholesterin, and the substance is most readily prepared from this source by extraction with hot alcohol. On evaporation, cholesterin is obtained as a crystalline mass which is soluble in alcohol, ether, and chloroform; from chloroform it crystallises in characteristic notched plates.

Tests.—The presence of *mucus* is recognised by the addition of *acetic acid*, which gives a precipitate.

The presence of *bile-acids* is recognised by *Pettenkofer's test.* This consists in the cautious addition of H_2SO_4, and of a few drops of cane-sugar solution, or a drop of furfural solution; a purple colour signifies the presence of bile-acids.

The presence of *bile-pigments* is recognised by *Gmelin's test.* Nitric acid (containing also nitrous acid as indicated by red fumes) causes a play of colours from green to blue, violet, red, and yellow.

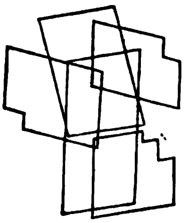


FIG. 77.—CHOLESTERIN. NOTCHED PLATES.

Cholesterin is recognisable (*a*) under the microscope by the crystals which are formed in its chloroform solution, (*b*) by the addition of sulphuric acid to a chloroform solution giving a bright cherry-red colour.

Pancreatic juice is a viscid albuminous secretion of high specific gravity, and of alkaline reaction. The amount secreted per diem does not exceed 150 c.c., *i.e.* it is about $\frac{1}{10}$ the amount of bile secreted per diem. It contains:—

	per 100
Water	90
Albumin	10
Ferments, namely, lipolytic, proteolytic, and amylolytic	
Salts, especially Na_2CO_3	

Tests.—*Albumin* is recognised by boiling. The amount of albumin is often so large that the fluid is coagulated *en masse.*

Ferments are recognised by the changes which take place in appropriate digests, (1) of fat, (2) of proteid, (3) of starch, with pancreatic juice or with pancreatic extract. Fatty acid appears in the first digest, peptone in the second, sugar in the third. Stale pancreatic juice contains products of the digestion of its own albumin, viz. peptone, leucin, and tyrosin.

USES OF THE BILE AND OF PANCREATIC JUICE.

Bile is mainly a digestive fluid, *i.e.* it is a secretion to be further utilised in the body, not merely an excretion to be forthwith expelled. The simple anatomical fact that the bile-duct enters the intestine at its very beginning, is enough to prove this point. A no less simple physiological experiment confirms the view; if in a dog, for instance, a biliary fistula is made through which bile is diverted, the animal thins rapidly, and by the eagerness he evinces to lick bile from the fistula, says plainly enough that bile is wanted; the rapid emaciation in spite of an ample diet, and the fatty nature of the fæces discharged, informs us further that bile is wanted for the *digestion of fat*, since, failing the bile, fat passes undigested and unabsorbed along the intestinal canal. It should be added, however, that the malnutrition caused by loss of bile seems to be far less serious on the human subject; what occurs in a dog does not necessarily apply to man; perhaps the difference may be partly due to the fact that human bile contains very little of the sulphur-holding principle—taurocholic acid, whereas in dog's bile it is *the* bile-acid.

Bile is also to a small extent an excrement. Already during fœtal life, when it can have no digestive office, it is discharged into the intestine, where it forms part of the excrement termed *meconium*. In the adult most of the bile secreted by the liver does its work in, and is reabsorbed by, the intestine, but a small amount is not so reabsorbed, and escapes with the fæces, and another small amount, although reabsorbed, is separated by the kidneys with the urine. These excrementitious substances of bile form especially the colouring matters of fæces and of urine, *stercobilin* in the former, *urobilin* in the latter, both these substances being indistinguishable from *hydrobilirubin* (=reduced bilirubin).

We are not, however, at this stage concerned with the excretory action of the liver, but only with its secretory action, in so far as bile is a digestive fluid, and shall therefore only allude to the fact that as an excretory organ the liver forms substances which find their way into the blood, and are separated from it by the kidneys. We shall see in a future section that this physiological association between kidney and liver as excretory organs applies to urea and to uric acid, which are probably formed in the liver and carried away by the hepatic blood, as well as to bilirubin, which is carried away by the bile (p. 244).

In addition to its principal action upon fats the bile assists in digestion by precipitating syntonin, albumose, and pepsin, thus preparing the gastric chyme for the digestive action of pancreatic juice; bile also promotes the digestion of starch; it stimulates peristaltic movements, thus exercising a slight purgative action; and it retards the putrefaction of food in the intestine, thus exercising a slight antiseptic action.

The digestion of fats and of proteids and of carbohydrates is promoted by bile, the action on fats being, as already stated, the most important of the three; in each case the bile acts in concert with pancreatic juice, the relative action of the two fluids being essentially preparation by bile, completion by pancreatic juice. We have an anatomical token of this partnership in the close proximity or actual conjunction into one channel of the biliary and pancreatic ducts; physiological evidence of united action is afforded by the parallelism between the biliary and pancreatic secretions, which rise and fall together (fig. 79), pathological evidence by the fact that fatty stools, due to the non-digestion of fat, may result from liver disease alone, or from pancreatic disease alone, showing us that the healthy secretion of both glands is necessary to the digestion of fat.

Experiments outside the body fully bear out these statements. 1. *Experiments on fats.*—Bile and oil shaken together form a fine and permanent emulsion; this finely divided state is obviously favourable to digestion. Pancreatic juice and oil likewise form a good emulsion; pancreatic juice moreover effects an actual division of fat into glycerine and fatty acid. This division is in many ways favourable to digestion. The fatty acid, of itself, favours emulsification, and still more so by virtue of the fact, that by uniting with the sodium of the bile-salts it forms soap. The soap so formed not only favours emulsion, but it is itself diffusible through animal membranes, and its presence in their pores enables them to be traversed by fat as such. Thus bile and pancreatic juice acting together promote the absorption of fat by favouring its emulsification, its decomposition, and its saponification. The composition of fats and soaps will be found graphically represented in the Appendix.

Bernard's observation.—A most striking piece of evidence pointing to the part which the pancreas plays in the absorption of fat, was furnished by Bernard's observation on the rabbit. In this animal the pancreatic duct opens into the intestine about 30 cm. below the opening of the bile-duct; if a rabbit is killed two or three hours after receiving a fatty meal, and its mesentery examined, the lacteal vessels above and below the opening of the pancreatic duct will be found very different in appearance; in the portion of mesentery connected with the intestine above the duct, the lacteals contain clear lymph without fat, while below it they contain white chyle with an abundance of fat;

that is to say, fat is being absorbed only in the portion of intestine below the duct after the pancreatic juice has taken effect upon it.

2. *Experiments on proteids.*—The addition of bile to a gastric digest causes a precipitate of syntonin and of albumose and puts an end to the action of pepsin. In the body, these effects are probably the necessary antecedent to pancreatic digestion. The partially digested proteid contained in the acid chyme which is gradually pressed through the pylorus, requires to be acted upon by bile before it can undergo further digestion by pancreatic juice; in other words bile arrests peptic digestion in an acid medium, and prepares chyme for pancreatic digestion in an alkaline medium. This interference with peptic digestion, which in the duodenum is the normal event, can occur as an irregular event in the stomach; bile may be driven the wrong way from the duodenum into the stomach, where it interferes with digestion and produces vomiting. Pancreatic juice has a powerful digestive action upon proteids (Corvisart, Kühne), which it owes to the presence of the ferment *trypsin*; under its influence proteids are converted into peptones which are indistinguishable from gastric peptones. This digestive action on proteids differs from that of gastric juice in the following particulars:—(*a*) It occurs only in an *alkaline* medium. For a gastric digest we employed dilute hydrochloric acid ·15 per cent.; for a pancreatic digest the best medium to employ is a 1 per cent. solution of *sodium carbonate*. (*b*) The proteolytic power of trypsin is greater than that of pepsin; the latter does not carry proteid beyond the peptone stage; the former, besides converting proteid to peptone, can break up peptone, giving rise to *leucin* and to *tyrosin*, and at a latter stage to indol, phenol, and other bodies. (*c*) As subsidiary points of difference, it may be mentioned, that whereas in a gastric digest acid-albumin is an intermediate product, in a pancreatic digest it is alkali-albumin; and that when fibrin is used for such experiment it swells up before solution in the gastric fluid, while in the pancreatic fluid it is gradually corroded and dissolved. Moreover the great rapidity with which a pancreatic digest enters into putrefactive decomposition is characteristic; in a few hours it has a repulsive

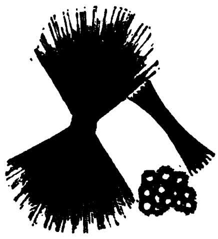


FIG. 78.—TYROSIN AND LEUCIN. SHEAVES AND LUMPS.

smell, and a drop of the fluid examined under the microscope is seen swarming with bacilli.

3. *Experiments on carbohydrates.*—Bile by itself has little or no digestive action upon carbohydrates: at most it has a slight amylolytic action, converting starch into sugar. The principal digestive agent of starch is pancreatic juice, which acts in this respect far more actively than the most active saliva. Soluble or even raw starch left to digest at 40° with pancreatic juice, or pancreatic extract, is rapidly converted into sugar of the maltose variety. The presence of bile seems to promote this digestion; if we compare two digests of starch and pancreatic extract, to one of which bile has been added, this last will be found to contain more sugar than the digest made without bile (Martin).

Reviewing the preceding experiments we see that the statement made at the outset to the effect that the combined digestive action of bile and of pancreatic juice is essentially preparation by the former, completion by the latter, is fully justified and applicable to all three classes of food principles, to proteids, to fats and to carbohydrates. Bile contains no ferments. Pancreati juice contains *lipolytic*, *amylolytic*, and *proteolytic* ferments, actin respectively upon fat, upon starch, and upon proteid.

For the sake of completeness, rather than because we hav any reason to believe that the action is normally exercised, i may be mentioned that pancreatic juice or extract possesses th rennet property of coagulating milk; we have, however, n ground for supposing that milk can ever escape coagulation i the stomach either by rennet ferment or by acid, and be coagu lated by pancreatic juice.

Derivation of the bile-substances.—The specific biliar substances (pigments and acids) are made by the liver, n simply removed by it ready-made from the blood. This is i contrast with what we shall find in the case of the kidney, whic simply separates from the blood ready-made urea produced b the tissues. What are the facts upon which the above doctri is based? Briefly stated they are as follows:—After removal the kidneys, urea accumulates in the blood; *i.e.* it continues be formed in the absence of the kidney; after removal of t liver, the biliary substances do not accumulate in the bloo *i.e.* the presence of the liver is necessary to their formation.

It must, however, be observed that the contrast is not actual as precise as set forth in the above curt statement. On the o hand, we have to admit that some of the specific urinary constituents are formed by the kidney; on the other, that some of the specific biliary constituents may be formed in the tissues. So that it is a nearer approach to the truth to say that a greater part of the bile-substances are made by the liver, a lesser part may be made by the tissues, while a greater part of the urinary substances are formed by the tissues, a lesser part by the kidneys.

Let us consider the case of the bile-pigments. The liver is one of the organs in which red corpuscles are destroyed, and the hæmoglobin derived from them is the source of the bile-pigment formed by the liver. Acting upon this liberated hæmoglobin, the liver forms bile-pigments. We have thus accounted for the greater part of the bile-pigments.

Blood effused into the tissues is found to have formed hæmatoidin by simple lapse of time (*e.g.* in old cerebral hæmorrhages); this is undoubtedly a blood-pigment, and it is indistinguishable from the bile-pigment bilirubin. Here we have a visible instance which leads us to admit that the tissues themselves, acting upon blood-pigment, can form a bile-pigment. This is a reason for admitting that a lesser part of the bile-pigments may be formed by the tissues.

Bile-pigment differs from blood-pigment in this important particular, that the former does not contain iron. We should accordingly expect to find—and in point of fact we do find—free iron salts deposited in the liver tissue; a slice of liver washed and immersed in a solution of potassium ferrocyanide (10 per cent.) for a few minutes, washed again and left in hydrochloric acid (2 per cent.) for a few hours, turns *blue*, indicating the presence of peroxide of iron. This free iron must come from hæmoglobin, which is broken up, partly in the liver, partly in the tissues generally; in the latter case it exists in the plasma as an albuminate of iron, which in order to give the blue reaction must first be oxidised by combustion or by boiling with H_2SO_4, and it is not improbable that some of the liver iron is formed from this source; according to Delépine the iron deposit is at its minimum immediately after a meal, at its maximum 6 to 8 hours later.

Extirpation of the liver yields very little information as to hepatic function, because cold-blooded animals and birds are alone capable of surviving the operation for any length of time. As regards mammalian animals we must have recourse to pathological observations. Obstruction of the bile-ducts leads to a accumulation of bile-pigments in the blood and in the lymph (the yellow discoloration so produced is called jaundice); wherea abolition of hepatic function does not lead to such accumulatio at all, or causes it in much less degree. In the first case, w have the obvious change brought about by an active liver wit its duct obstructed; in the second, we have the doubtful or negative consequence of diminished liver action. The conclusion i as before that bile-pigment is certainly and in large quantit formed by the liver, and that, failing the liver, it is possibly, an in small quantity, formed in the tissues of the body.

This amounts to saying that bile-pigment is normally forme by the liver; the association between bile-pigments and bile-acid is so constant, that we are justified in believing that what i true of bile-pigments is also true of bile-acids, and that the latt also are normally formed by the liver, not simply removed by i ready-made from the blood.

Biliary pressure.—The pressure to which the biliary secretio can reach, as measured by a manometer tied in the duct, is lo not more than 1½ cm. of mercury. This has important pra tical bearings, as well as some theoretical interest. It explai to us how slight a cause is sufficient to arrest the flow of bil and consequently give rise to its reabsorption and to jaundic A gall-stone in the duct will obviously enough produce the effec but it may be due to apparently far slighter causes; a swolle and congested state of the mucous membrane of the duodenu is a sufficient impediment, and a frequent cause of jaundice.

The theoretical interest attaching to biliary pressure lies i its comparison with blood-pressure. It has been remarked th the maximum biliary pressure of 1½ cm. Hg is much bel ordinary blood-pressure, so that the proof of secretory indepe dence given for salivary secretion does not cover the case biliary secretion; but it is to be remembered that the hepa blood-pressure is not that of the arterial system, but only th of the portal vein, which is equal to less than 1 cm. Hg.

There is no experimental evidence of any direct action of nerv upon biliary *secretion*, although the *expulsion* of bile from the ga bladder into the small intestine occurs in response to stimulati of the duodenum by the acid chyme; touching the duode opening of the bile-duct with a glass rod dipped in dilute a causes a gush of bile. The discharge of bile into the intesti is greatest about 3 to 5 hours and again at 13 to 15 hours after food. These two maxima of biliary discharge approximately coincide with maxima of pancreatic secretion, which occur soon after.

The direct action of nerves upon pancreatic secretion, although probable, is not supported by definite experimental evidence. Stimulation of the medulla excites the secretion; excitation of the central end of any afferent nerve has a contrary effect. Destruction of the nerves which are distributed to the pancreas interferes with the above-mentioned effect, and is followed by the establishment of a thin watery secretion analogous with the 'paralytic' secretion which occurs from the submaxillary gland after section of the chorda tympani.

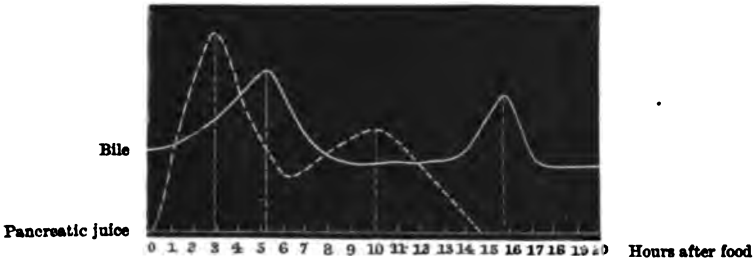


FIG. 79.

Curves of biliary and of pancreatic secretions subsequent to the ingestion of food.

But in the case of pancreatic as in that of biliary secretion, the experimental isolation of secreto-motor nerves has entirely failed; we have no right to say that the increased and diminished secretion are independent of the increased and diminished vascularity with which they are always associated. We must be content to recognise in these cases the simple fact that increased secretion is associated with greater blood-supply, diminished secretion with smaller blood-supply, without attempting to lay down whether the associated changes bear a relation of cause and effect, or whether both are or are not the double effect of a common cause. Thus with regard to any direct action of nerves upon pancreatic and biliary secretion, matters stand very much in the same position as in the case of gastric secretion—viz. the existence of modifications of secretion by nervous influence is indicated as possible by pathological considerations as well as by certain rough results of experiment; for instance, the pancreatic and biliary secretions are accelerated in response to the stimulating effects of swallowed food, and according to Heidenhain, stimulation of the spinal bulb distinctly augments the flow of pancreatic juice; but no undeniably direct secreto-motor action comparable with that of salivary nerves has ever been proved by the excitation of pancreatic, gastric, or hepatic nerves, and the possibility therefore remains that such effects as are observed are the indirect consequences of alterations of blood-supply.

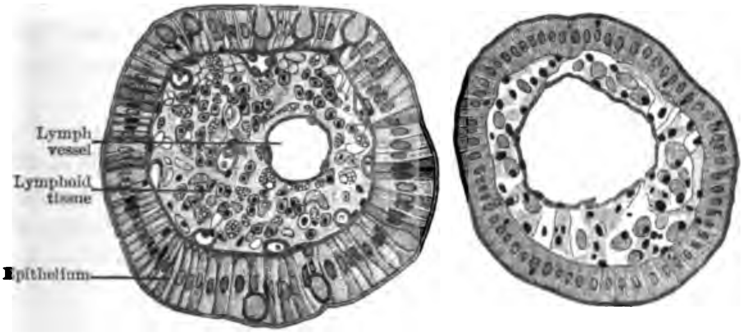
THE SMALL INTESTINE

The mass of chyme undergoing digestion is gradually propelled along the small intestine; this tube, if it were cut open and laid out flat, would occupy a large surface—about ½ square meter—and this already considerable surface is made still greater by the multitude of projections—valvulæ conniventes and villi—with which it is beset; 10 square meters is a fair estimate of the total superficial area of the small intestine. The chyme is thinly spread—'smeared over' this large surface, a condition which is eminently favourable to absorption. *Absorption* indeed is the chief function of the small intestine, further digestion by intestina fluid is its very subordinate function.

The wall of the small intestine is composed of the four coat already alluded to, viz. mucosa, submucosa, musculosa, and serosa. From the physiological point of view, the most important feature to be considered is the minute anatomy of th villi, which constitute the organ of absorption; attention should also be paid, (1) to the presence of Lieberkühn's follicles which furnish the intestinal juice; (2) to the fact that lymphoid tissu enters largely into the composition of the mucous and submucou coats, especially in the ileum where clusters of lymphoid nodule (Peyer's patches) are a prominent feature; and (3) to the fac that in the duodenum the submucous coat is occupied by a shee of gland tissue (Brunner's glands), which is histologically identica with salivary gland. The physiological action of the nervou tissue which forms the plexus of Meissner in the submucous coa and the plexus of Auerbach between the two muscular coats, entirely conjectural.

The villi are the principal instruments of absorption. The number has been estimated at 4 to 5 millions, and it has bee calculated that each square centimeter of intestinal surface increased twenty-fold by the villi which cover it. Their distribution is, however, far from being uniform, villi being longer, closer, and more numerous in the upper, than in the lower portions of the small intestine. A villus is composed of epithelium and lymphoid tissue; it contains blood-vessels, lymphatics, and possibly nerves, also plain muscular tissue derived from the muscularis mucosæ. The amount of lymphoid tissue in a villus of a flesh feeder (dog or cat) is much greater than in that of a vegetable feeder (rabbit or guinea-pig.)

By virtue of its muscular tissue a villus is contractile; in the relaxed state it is elongated, in the contracted state it is quite short; in consequence of the more or less stretched condition of the epithelial coat, according as the villus is relaxed or contracted, the individual cells are shorter and broader in a relaxed villus, longer and narrower in a contracted villus. According to Heidenhain the adenoid tissue of the villi contains a large proportion of granular lymphoid cells peculiar in their behaviour to staining reagents and to osmic acid. They are blackened by the latter reagent, and it might therefore be supposed that the granular material in the cells is fatty; but that this is not so, is shown by the fact that it is not dissolved out by ether. These cells are far more numerous during digestion than in the fasting state. They have been made responsible for the absorption of fat; but, as has just been stated, this is denied



Dog. Fig. 80. Rabbit.

Transverse sections of villi of carnivorous and of non-carnivorous animals. (Heidenhain.)

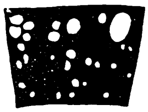


Fig. 81.

Intestinal epithelium taken during the absorption of fat, treated with ether and exhibiting vacuoles. Heidenhain.)

by Heidenhain. Fat is absorbed by the epithelial cells them selves; that this is so, and that it does not pass betwe the cells nor is carried by the leucocytes, is shown by treatin sections with ether, which dissolves the droplets of fat, leavin distinct vacuoles in the epithelial cells, while it has no actio on the granular lymphoid cells which are stained by osmic aci (Heidenhain).

The crypts of Lieberkühn are lined by epithelium, which a first sight appears identical with that which covers the villi they are not however on that account to be regarded as agents absorption. They are in reality secreting glands. The epitheli cells of the crypts, as compared with those of the villi, stain mo deeply and possess a much less distinct striated border; the nuclei frequently exhibit karyokinetic figures which are hardl ever observed in the nuclei of cells lining the villi.

Intestinal juice, secreted by the glands of Lieberkühn (and the glands of Brunner in the duodenum), is an alkaline fluid wi a specific gravity of 1010, having only a very slight digesti action upon the food-stuffs. Its most characteristic effect is t conversion of *cane-sugar* (saccharose) into *invert-sugar* (levulo + dextrose), by virtue of the ferment called *invertin.*

$$\underset{\textit{Saccharose}}{C_{12}H_{22}O_{11}} \underset{+}{+} \underset{\textit{water}}{H_2O} \underset{=}{=} \underset{\textit{levulose}}{C_6H_{12}O_6} \underset{+}{+} \underset{\textit{dextrose}}{C_6H_{12}O_6}$$

Intestinal juice has usually been obtained from an intesti fistula—formed by cutting out from the tube a portion which made to open externally, the cut ends of the main tube bei brought together so as to restore its continuity. The isola portion left in connection with its mesentery may be closed one end, the other end being sutured to the abdominal wound ultimately forms a blind sac with a single opening (Thiry's meth or both ends may be made to open at the surface of the abdom (Vella's method).

An experiment by Moreau is quoted to show that ne exercise some influence on the secretion of intestinal juice. portion of intestine drawn out of the abdominal cavity is s divided into three compartments by means of four equidist ligatures; the nerves of the middle compartment are divided the intestine replaced in the abdominal cavity. A few hours l the contents of the three compartments are examined; the mi compartment is found to contain a considerable quantit watery fluid, the two other compartments are almost empty. The effect, which may however be either a vascular or a direct secretory phenomenon, is comparable to that obtained on the salivary gland after section of the chorda tympani (paralytic saliva).

Before passing on to the consideration of intestinal absorption, opportunity may be taken to mention two important pathological relationships of intestinal glands. The glands of Brunner, of which we possess little or no physiological knowledge, are particularly prone to excessive action, going on to inflammation and to ulceration, in consequence of burns or scalds affecting any large extent of the cutaneous surface. The lymphoid patches of Peyer are particularly, it may even be said regularly, subject to inflammation and ulceration in the course of typhoid fever.

Absorption goes on in the whole intestinal tract—in the mouth, in the stomach, in the small and in the large intestine. It is at its maximum in the small intestine, in its upper portion more especially. Nearly everything that gets into the body does so by the surface of the upper part of the small intestine, after having undergone the digestive action of saliva, of gastric juice, of bile, and of pancreatic juice. We have already alluded to the fact that the conditions of absorption are (1) the diffusibility of the substance to be absorbed, (2) the physiological activity of the epithelium through which it is being absorbed. We have no right to say that either factor is the more important, but we have sufficiently realised the importance of the physical factor, and may therefore now insist upon the importance of the epithelial factor by adding to the illustrations already given of its efficacy (p. 158). Brücke long ago pointed out that egg-albumin can in part be absorbed as such unchanged, and his statement has found a practical application in the feeding of infants by raw white of egg. Voit and Bauer have determined that proteid solutions injected into the small intestine and into the rectum are actually absorbed, and the fact is no more than definite and exact proof that nutrient enemata are in reality nutrient. Bernard showed that if ferrocyanide and iodide of potassium be injected into a vein, the ferrocyanide passes into saliva and pancreatic juice, the iodide into the urine and bile; this is an illustration of the selective activity of epithelium—not indeed in absorption but in secretion—under identical physical conditions. Reid more recently has given exact proof of epithelial activity in the absorption through frog's skin, by showing that the osmotic current, which is normally greatest from outer to inner surface of the living skin, is hastened by a stimulant (alcohol), retarded by a depressant (chloroform). Cazeneuve and Livon have shown that the living epithelium of the bladder forms a barrier to the absorption of urea. We may sum up the function of the intestinal epithelium by saying that it furthers the absorption o favourable or feeding material, while it opposes the absorption o unfavourable or non-feeding material: its removal, so far from facilitating, would obstruct the absorption of food.

The channels of absorption are, (1) the blood-vessels, (2) th lymph-vessels, with which as we have seen the villi are abundantl provided. The materials, the absorption of which we are t inquire into, are water, proteids, fats, carbohydrates, and salts.

Röhmann's observations on the rate of absorption are to th effect that about 1 cubic centimeter of fluid passes through square centimeter of intestine per hour. Taking the villi int account, 1 sq. cm. of intestine has a surface of about 20 sq. cm and the speed of the absorption current through the epitheliu will be about ·5 mm. per hour or 8 μ per minute, *i.e.* a give particle of fluid traverses the epithelial layer, which is 30 t 40 μ in thickness, in about 5 minutes. Or otherwise calculated- 1 sq. centimeter covered by about 2,500 villi, each with a su face of ·9 sq. mm., gives a total absorbent surface of 22·5 sq. cm and a velocity of absorption of 7·5 μ per minute.

We have sufficiently insisted upon the importance of t epithelium; with regard to lymphoid tissue, the part it plays absorption is more obscure; it probably acts as a filter arresti the entrance of deleterious substances, or at least preventing th sudden entrance in mass, and giving time for their subseque gradual elimination. In correspondence with this view we fi a sheet of lymphoid tissue forming part of the absorbent surfa in the villi, in the submucous layer, and collected into nodules the solitary and in Peyer's glands; we moreover find that sh in its highest development in the large intestine, where the abs bent surface is most exposed to decomposition products; a finally on the course of the larger lymphatics we find a sec line of probable filtering organs, the mesenteric glands.

The respective functions of the blood-vessels, and of lymph-vessels as channels of absorption, are briefly to following effect: the greater part of the water, salts, sugar, and proteid absorbed, passes into the blood-vessels, and by the portal vein through the liver; the greater part of the fats absorbed passes into the chyle-vessels, and by the thoracic duct into the general venous system. In other words, the portal system is the chief channel of the absorption of water, salts, sugar, and proteid; the chyliferous system is the chief channel of the absorption of fats. We are nevertheless bound to admit that this distribution of function is not completely rigid; some small proportion of the water, salts, proteid, and sugar does enter the chyle-vessels, some small proportion of fat does enter the portal system.

It is highly probable that the liver plays towards the portal blood a filter or sentinel function, in arresting deleterious substances, like that played by lymphoid tissue and lymph-glands in relation to chyle. But this office is indicated only by pathological considerations, not by any definite experiments, and we did not therefore include it in the formal enumeration of liver functions.

We have now to follow as far as possible the internal digestion or the elaboration of the absorbed products of external digestion, and to answer the question—what happens to proteids, to carbohydrates, to fats, &c., when they have got into the body. We have studied the entrance of the proximate food principles, and the preliminary transformations which they undergo; we can study their exit and the forms which they then assume, viz. carbon dioxide and urea; our present task is to study the chemical metamorphoses occurring between these two extremes. We shall find that with the exception of the glycogenic function of the liver, only the most fragmentary glimpses can be obtained of what takes place in the depths of the tissues.

GLYCOGENESIS.

The great importance of the glycogenic function of the liver is owing partly to the considerations just alluded to, partly to the fact that this function, while localised in and exclusively undertaken by the liver of fully organised animals, is a function common to many tissues in the embryo, and essentially similar to the starch-function in vegetable tissues. We shall therefore consider:—

(1) Its nature as manifested by the liver of an adult

mammal. (2) Its distribution in the animal scale and in fœta tissues. (3) Its relation to food, health, and muscular action.

The glycogenic function of the liver was discovered by Claud Bernard in 1848. He was making experiments to determin where sugar is consumed in the organism, and in the course o these experiments he analysed the blood going to and comin from the liver, and found that the blood of the hepatic vei contained more sugar than that of the portal vein; from whic he concluded that the liver produces sugar. Thus while lookin for the seat of sugar-consumption, he found a seat of sugar production. This was the first step. About ten years late Bernard supplemented his first discovery by finding that th liver contains a substance very like starch, which like it is con vertible into sugar by ferment action, and which he therefor named 'glycogen.' This was the second step.

From these observations we learn that the liver can mak sugar and can make glycogen, and recognise that the sugar-pro ducing or glycogenic process consists of two stages:—(1) The fo mation of glycogen. (2) The conversion of glycogen into gluco

Objections.—That the liver *normally* produces sugar was n at once accepted as unquestionable. Bernard himself had show that an excised liver can produce sugar *post mortem*; he showe that a liver washed sugar-free and left to itself, is after a tim found to contain a fresh supply of sugar. Pavy thereupo urged that the formation of sugar is not a normal physiologic event, but only a *post-mortem* occurrence. He objected Bernard's analyses of hepatic and of portal blood, that the hepat blood had been allowed to stagnate in the liver, whose functi was thereby disordered, and stated that normal hepatic blo contains no more sugar than normal portal blood. The ca stood as follows:—According to Bernard, the liver is constant forming sugar during life and continues to do so after excisio during life the sugar is carried off from the liver as fast as it formed, so that a perfectly fresh liver is almost or quite suga free, while a stale liver contains an abundance of sugar. A cording to Pavy, it was not legitimate to conclude that the liv makes sugar normally in the body, because it is found to do abnormally out of the body. The crucial point is the compar tive analysis of portal and of hepatic blood. Do the two kinds blood taken simultaneously from the two vessels without previo arrest of the hepatic circulation, exhibit any difference in t amounts of sugar they respectively contain? Recent analyses show that they do, and that the average amount of sugar in portal venous blood is 1 per 1,000, in hepatic venous blood 2 per 1,000. The conclusion is therefore justified that the liver produces sugar in the body during its life as well as out of the body after the circulation has ceased. If we take into account how great is the quantity of blood passing through the organ per hour or per day, we must recognise that the small difference between 1 and 2 per 1,000 is significant of a very large daily production of sugar. Seegen, for instance, has estimated that more than 400 litres of blood pass through the liver of a 40 kilo dog in one day, which, taking the sugar produced at 1 per 1,000, gives a daily production of over 400 grammes. This estimate is possibly an exaggerated one; still there can be no doubt that the daily sugar production by the liver is very considerable. With regard to the immediate antecedent of sugar, it is admitted by all authorities (with the exception of Seegen, who positively asserts that the liver can form sugar directly from either proteids, fats, or carbohydrates), that the liver-sugar is exclusively derived from glycogen.

Source of glycogen.—We have now to consider the derivation of glycogen. Is it derived from proteids, or from fats, or from carbohydrates, or from all these three classes of foods? The answers to these questions are as follows:—

1. That it is derived from food, because in the absence of food the liver contains no glycogen.

2. That it is derived from carbohydrates especially, because animals fed upon exclusively starchy or saccharine food accumulate much glycogen in their livers.

3. That it is also derived from proteids, because animals fed upon exclusively proteid food form glycogen in their livers. This, the cardinal fact of the whole debate concerning the source of glycogen, was for long the subject of dispute, and has only been determined by prolonged and repeated experiments. As originally conducted the observations were carried out on dogs fed upon horseflesh, which was assumed to be purely proteid, but which was subsequently found to contain a minute amount of glycogen or dextrine. The objection to which this gave rise has however been disposed of by the use of other kinds of meat free of all carbohydrate.

4. That it is not derived from fat, because animals fed upon an exclusive diet of fat, possess no glycogen in their livers.

Thus as regards the formation of hepatic glycogen we have the following order of efficacy: carbohydrates most—proteids some—fats not at all.

The most important of these facts is that the nitrogenous proteids do give rise to the non-nitrogenous glycogen. It is strikingly exemplified in the pathology of diabetes, the essential symptom of which consists in the passage in the urine of a suga with which the liver-sugar is identical. A subject of sever diabetes on ordinary diet (containing proteid, fat, and carbohydrate) passes an excessive amount of sugar, on a restricte diet (containing proteid and fat, but no carbohydrates) a smalle but yet a considerable amount of sugar, which must, therefore be derived from proteid.

Preparation of glycogen.—The preliminary condition is th choice of an animal with the liver in a highly glycogenic conditio In correspondence with what has been said as to the influence o diet, we should not expect to find glycogen present in the liver o a starving animal, nor should we expect to get much glycoge from the liver of a carnivorous animal unless specially diete The liver of a vegetable-feeding animal in full digestion of ca bohydrate will give the largest amount of glycogen; therefo select a rabbit two or three hours after a large feed of carrots; th liver of such an animal is large, pale, and friable, and may contai from 5 to 15 per cent. its weight of glycogen. Moreover, havin learned that glycogen is rapidly transformed into sugar *po mortem,* we remove the liver *immediately* after death, and arre the transformation by plunging it into boiling water, cutting tearing the organ in pieces as fast as possible. Under the conditions we shall find in solution a minimum quantity of sug and a maximum quantity of glycogen. The boiling is continu for 15 to 20 minutes, the liver-tissue being further subdivided a finally pounded with sand to ensure the extraction of all availab glycogen. The mess is filtered and yields a milky opalesce solution of glycogen, mixed with some proteid and some fat. Fro this solution proteid is removed by precipitation with Brücke fluid (potassio-mercuric iodide) and dilute hydrochloric aci added alternately in small quantities until no further precipitate produced. From the filtrate the glycogen is precipitated by t gradual addition of twice its volume of ordinary alcohol. T precipitate is collected upon a filter and washed, first with alcoh then with ether to remove fat, finally with absolute alcohol.

The glycogen precipitate, dried over sulphuric acid, yields on pounding, a bulky white amorphous powder, soluble in water, with which it gives an opalescent solution; this solution gives a red or brown colour with iodine, which disappears on heating and returns on cooling. As implied by its name, and by the synonym 'animal starch,' it is a carbohydrate body closely resembling starch and dextrin, convertible into the same product—sugar, and represented by the same empirical formula—$C_6 H_{10} O_5$.

We have considered the formation of glycogen, we have now to consider its fate, and the part it plays in the body. We have already reviewed the influence of diet upon the glycogen formation in the liver; with regard to the influence of health and of exercise, the principal facts are that *cæteris paribus* an animal in good health, or a quiescent animal, or any hibernating animal, such as a frog at the outset of winter, has a liver with glycogen, while an animal in bad health, or an active animal, has a liver without glycogen. If, for instance, we look for glycogen and for sugar in the liver in the following cases, we should find:—

1.	In a liver from the post-mortem room	no glycogen	no sugar
2.	„ a butcher's stall	no glycogen	sugar
3.	„ a recently killed tame rabbit	glycogen and	sugar
4.	„ a hunted wild rabbit	no glycogen	no sugar

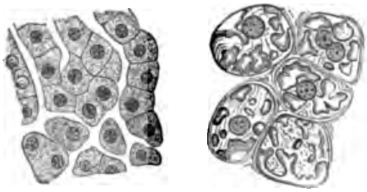
These facts involve a consideration of the physiological relation between glycogen in the liver, sugar in the blood, chemical changes in the tissues. Sugar is a constant constituent of the blood, which in a starving or a well-nourished animal alike contains about 1 per 1,000 of sugar. The amount of sugar present in the venous blood of muscle is constantly slightly below that present in arterial blood, and the amount present is at its minimum in the venous blood of active muscle. Sugar is therefore consumed by living muscle, especially during activity. The amount of sugar present in hepatic venous blood is constantly slightly above that present in portal venous blood. Sugar is therefore produced by the liver. We have now no difficulty in following the sugar-cycle in an active well-fed animal. Absorbed sugar enters the blood, is to a great extent stored as glycogen in the liver, is consumed by living muscle, is discharged as CO_2 and as H_2O. The part played by glycogen is that of a temporary carbohydrate reserve.

In a starving animal, receiving no fresh supply of sugar,

sugar is nevertheless a necessity; the glycogen store soon disappears; yet the animal lives on for a time, having sugar in it blood, and using up sugar in its muscles. It is probable tha this sugar is made *by* the tissues *from* the tissues (by the liver an possibly by muscle, from proteid and possibly from fat). Fro this point of view the fundamental chemical event is the formatio and consumption of sugar; the formation of glycogen is a fir incident in this event, occurring whenever the carbohydrat supply is plentiful, and failing to occur when the food-supply suspended.

It is instructive to observe that this reserve carbohydrat function is represented throughout the animal and vegetab kingdoms; the liver makes and puts by glycogen at one tim transforms and discharges glycogen at another time; a potat makes and puts by starch at one time, transforms and discharg starch at another time. The alternate phases are of very di ferent duration in the different cases; the carbohydrate reser remains for a few hours or days in the liver of a warm-bloode animal, for many days or weeks in the liver of a cold-bloode animal, for several months in the tuber of a potato, or in th liver of a hibernating animal.

Alterations of the liver-structure in consequence of digestio are obvious enough both to the naked eye and microscopicall but the interpretation of the significance in all their visib details is rendered uncertai mainly because we have to de with two possible altering agen —with an outgoing current secretion as in other glands, a with an incoming current food-products. It is to the las named factor that the mo obvious changes are due. Tl liver of a rabbit dieted in pr paration for glycogen extraction, is large, pale, and twice as hea as the liver of a similar rabbit not so prepared; and where the liver of the fed rabbit may yield over 10 grammes of gl cogen, that of the other rabbit would yield less than 1 gramm A microscopic section of a dog's liver during the fasting sta shows uniformly granular shrunken cells with obscured nucl



FASTING. FIG. 82. AFTER FOOD.

Liver cells of dog after a thirty-six hours' fast, and fourteen hours after a full meal—in the latter case swollen with glycogen. (Heidenhain.)

taken twelve or fourteen hours after a copious meal, the cells are distended with coarse clumps, which give a red-brown colour on irrigation with iodine, and which, when they dissolve, leave the cells with distinct boundaries and distinct nuclei in a ragged intra-cellular network of protoplasm. The appearance is evidently due to a deposition of and distension by glycogen during the post-prandial period.

Changes in the main similar to the above and attributed to the glycogenic process, have also been made out upon frogs, in which the liver is of distinctly tubular type. According to Langley, the liver of a winter frog exhibits a distinction into zones similar to those of the salivary glands; in this case the outer hyaline zone is loaded with glycogen, the inner granular zone with material, presumably proteid, but which, seeing that the liver yields no definite ferment, cannot be termed 'zymogen.' Another material which is apt to be deposited in the liver-cells, both of mammalia and of frogs, is fat, which forms droplets more or less abundantly in accordance with the state of nutrition (*e.g.* the fatty livers of crammed geese or of over-fed and ill-nourished persons), but in no causal relation with the particular phase of digestion. Finally we have to recognise that the hæmolytic function of the liver may be attended with visible changes. According to Delépine, a granular deposit giving the ferric reaction exists in the liver-cells—slightly during fasting, not at all immediately after a meal, most abundantly six to eight hours later.

Diabetes.—The essential phenomena of diabetes are the passage of sugar into the urine, and an excessive discharge of water. The first event is the characteristic of *diabetes mellitus*, and is found to be associated with the presence of an excessive amount of sugar in the blood; the second event is the characteristic of *diabetes insipidus*. No conclusive proof has yet been given to show that the urine normally contains any sugar, and it is certain that normal urine does not contain it in considerable amount; in a case of *diabetes mellitus* the urine may contain as much as five per cent. The average percentage of sugar in normal blood is only ·1; the percentage of sugar in diabetic blood may reach ·5. Comparing these two amounts, ·5 per 100 in blood, 5 per 100 in urine, we recognise that mere diffusion will not account for the excretion of sugar, but that, as in the case of urea, an activity of renal epithelium must be invoked.

The excess of sugar in the blood, disposed of by the kidney, is attributable to two causes:—(1) abnormal action of the liver, (2) deficient consumption by the tissues, and it is probable that both causes contribute to the result. The abnormal action of the liver can be regarded in two different lights; either the live action is defective, sugar coming from the intestine is not stored as glycogen; or the liver action is excessive, more suga than usual is made. The second alternative is the more probable; diabetes is not produced by diseases in which liver actio is certainly defective, and it may persist, though in diminishe degree, when all starch and sugar are withheld from th dietary.

The relation between excessive action of the liver an diabetes is further borne out by the effects which follo puncture of the spinal bulb, and several other operation Rabbits shortly after a puncture of the fourth ventricle becom diabetic in so far as they pass sugar in the urine. Frogs sim larly treated, especially at the beginning of winter, are similarl affected. This diabetic state is, however, temporary, and a essential condition of its appearance is that the liver shal at the time of puncture, contain a large store of glycogen. appears therefore that *puncture diabetes* is due to an accelerat conversion of liver-glycogen into sugar. This view is borne o by further observations; it has been found that several oth operations will produce the same result, *e.g.* section of t cervical sympathetic or of the spinal cord, destruction of t cervical or of the stellate ganglia, excitation of the central e of the vagus, or indeed of any afferent nerve, ether, morph apnœa, and, finally, the injection of arterial blood into the port vein; the common effect in all these cases, viz. sugar in t urine, being attributable to one common cause, viz. to hyperæm of the liver. It should be added, however, that the sugar action may be simulated by the allied carbohydrate, glycuro acid, $C_6H_{10}O_7$, which according to Ashdown is the substan giving the apparent sugar reaction in the urine of chlorofo narcosis. Puncture of the bulb may also give rise to *diabe insipidus*; this effect, the mechanism of which is more obscu is attributable to vasomotor disturbance of the kidney rat than of the liver.

Recent experiments have shown that the pancreas bears some pecul relation to the sugar function; dogs are said to be rendered diab by complete removal of the pancreas, the diabetes so produced remaining permanent until death (Minkowski and v. Mering), contrasting in this respect with the temporary character of *puncture diabetes*; the nature of the relation between diabetes and loss of the pancreas is as yet entirely obscure; it is comparable with the equally obscure action of the thyroid gland, *i.e.* in both cases removal of a gland causes a peculiar malnutrition, characterised by excess of sugar if the pancreas is removed, by excess of mucin (myxœdema) if the thyroid is removed; in both cases, therefore, the gland in question must be of importance to healthy nutrition; this is not the place to discuss at length the possibilities which are suggested by observations of this order; it is enough for us to recognise that a relation—however obscure—really subsists between the special functions of particular organs, and the general nutrition of the body. These are modern examples of the conception long ago formed by Treviranus, to the effect that the several parts of the body are mutually interdependent, the waste of one organ serving as the raw material to another organ, and even the organs themselves being conceivably 'excretory products' in relation to the remainder of the organism. The development of the mammary gland coincident with the presence of a fœtus, the arrested development of male characteristics in consequence of castration, may also be pointed to in token of the obscure inter-organic relations which play a part in the internal economy of the processes of nutrition.

CHAPTER VI

RENAL EXCRETION

PAGE
222 The relation of excretion to digestion.
223 The kidney.
227 THE URINE—quantity—reaction—specific gravity—composition.
228 MECHANISM OF ITS SECRETION. Theories—of Bowman—of Ludwig—of Heidenhain—'Water through glomeruli, urea through tubules'—Observations of Heidenhain—of Nüssbaum—Effects of blood-pressure—of state of blood—of nerve-action—Use of the renal oncometer.—The renal nerves.
233 UREA—'Made by the tissues, discharged into the blood, separated by the kidneys'—'formed in chief part from food proteid, in small part from body proteid'—Proofs of these statements.
235 Detection, preparation, synthesis, and estimation of urea—Hypobromite method—Distillation method.
237 Uric acid—Hippuric acid—Creatinin—Salts—Chlorides, phosphates and sulphates—Pigments—Urobilin.
241 *Abnormal constituents*—Blood, albumin, and sugar—Estimation of sugar by copper, by fermentation, by the polarimeter.
243 Micturition—vesical pressure.
244 Excretory action of the liver.
246 Excretory action of the skin.
247 Effects of partial excision of kidney.

The relation of excretion to digestion.—Respiration, digestion, circulation, and excretion are the agencies through which the blood is maintained of such quality and composition, that it serves throughout life as the vehicle of nourishment and of purification to the whole body. Respiration is essentially a process of exchange, formed by a double current of gases—of incoming oxygen, and of outgoing carbon dioxide. Digestion and excretion similarly constitute a process of exchange, in which, however, the two currents run in separate channels; carbon and nitrogen entering the body together by intestinal absorption, but nitrogen leaving the body by renal excretion as urea, and carbon by respiratory excretion as CO_2. And whereas in the absorption of oxygen, the gas exists ready in the air and enters the body unaltered, carbon and nitrogen are conveyed into the body in certain combinations or proximate principles (carbohydrates, fats, and proteids) which form part of our ordinary articles of diet, and require to be prepared for absorption by digestion in the alimentary canal before they can actually enter the body. Thus respiration is simple absorption and excretion of gases, digestion is the preparation for absorption, and actual absorption of proteids, of carbohydrates, and of fats. Indigestible substances simply pass through the alimentary canal without actually entering the body, and are got rid of by defæcation, in company with an insignificant amount of matter actually excreted by the intestinal canal. The principal excretions, properly so called, are CO_2 by respiration, and urea by renal action. We have already considered the former, we are about to consider the latter.

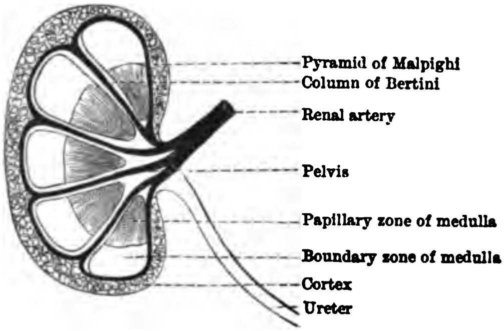


FIG. 83.—DIAGRAMMATIC SECTION THROUGH THE KIDNEY.

The branches of the renal artery pass along the columns of Bertini and form a series of arterial arches between cortex and medulla; from these arches spring the interlobular arteries and the vasa recta. (See fig. 85.)

The kidney.—A human kidney sliced longitudinally exhibits an outer zone—the cortex—surrounding an inner portion—the medulla. The medulla is composed of twelve to fifteen pyramidal masses; its outer portion in contiguity with the cortex is called the boundary zone; its inner portion is termed the papillary zone, each pyramid terminating as a papilla which protrudes into the pelvis of the kidney; the pelvis is the common central cavity and the commencement of the ureter. The structural character of the several portions of the kidney are determined by peculiarities in the anatomical disposition of (1) the blood-vessels, (2) the urinary tubules. Microscopically, the cortex is characterised by convoluted tubules in such mass as to be termed the 'labyrinth;' it also contains bundles of straight tubules forming the medullary rays. The boundary zone of the medulla is characterised by looped tubules, the papillary zone by converging tubules. In an injected kidney the cortex is characterised by the presence of capillary 'glomeruli,' the boundary zone by the presence of a straight system of capillaries; the cortex contains also a rich network of capillaries around the convoluted tubes; the papillary zone of the medulla is on the contrary very scantily supplied by capillaries which are derived from the vasa recta. As in all secreting or excreting glands, the essential elements are a thin sheet of *blood* separated by a *membrane* from a layer of *epithelial cells*. In the case of the kidney the blood is contained in the capillaries forming the glomeruli and surrounding the tubules, the epithelium covers the glomeruli and lines the tubules.

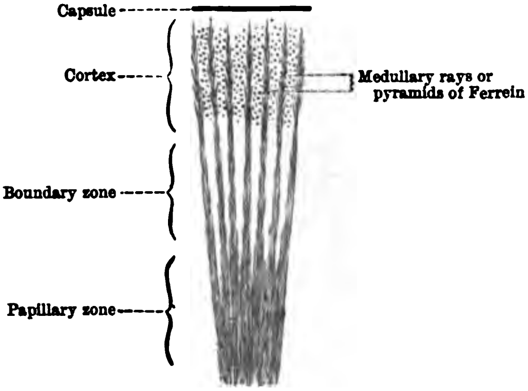


FIG. 84.—DIAGRAMMATIC SECTION THROUGH A PORTION OF THE KIDNEY

The renal artery enters at the hilum and divides at once into several main branches which run between the pyramids towards the cortex; at the junction between medulla and cortex the branches form incomplete arcades from the two sides of which spring the smaller vessels supplying the labyrinth (interlobular vessels) and the boundary zone (vasa recta). From each side of an interlobular artery spring several short branches (afferent vessels) each of which breaks into a tangled bunch of capillaries constituting a glomerulus; the minute veins (efferent vessels) formed from these capillaries do not at once unite with other veins, but first undergo redistribution as a second capillary network surrounding the convoluted tubes; some of these efferent vessels, springing from glomeruli close to the boundary zone, form a second capillary network in that zone (false vasa recta). The peculiarity of the renal circulation consists in this double capillary network—a first capillary distribution forming the glomeruli, a second capillary distribution, after the manner of a portal vein, forming the vascular network over the tubules. The disposition is similar in principle though not in detail with that found in the kidneys of amphibia, where glomeruli and tubules are supplied by distinct vessels—glomeruli by the renal artery, tubules by the renal portal vein (which is itself a branch of the femoral vein).

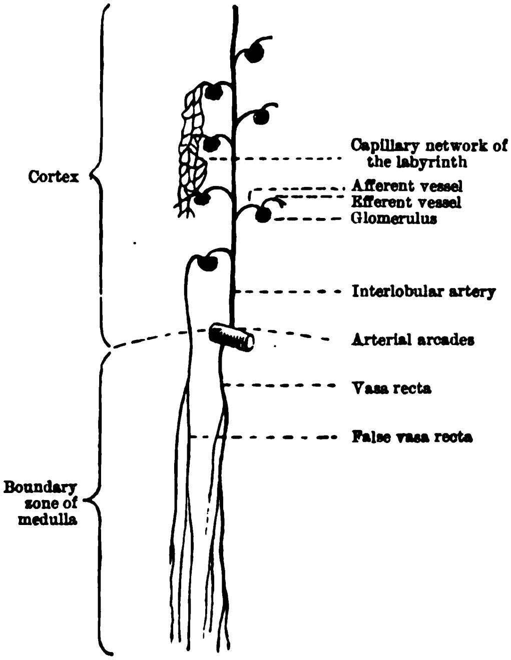


FIG. 85.—DISTRIBUTION OF RENAL ARTERIES.

A urinary tubule commences by a capsule (Bowman) surrounding and reflected over the glomerulus. From this commencement to its end at a papilla, it runs a very complex course, and is lined by epithelium of very varying appearance. Omitting details of purely morphological interest, the course and character of a tubule are as follows. The glomerular capsule is composed of two layers, the inner of which covers and is fused with the glomerular loops, while the outer layer is continued as the tube itself. This tube while in the cortex is convoluted, in the next portion of its course it forms a loop (Henle) occupying the whole breadth of the boundary zone of the medulla; in this loop we have to distinguish physiologically as well as morphologically the broad ascending from the narrow descending limb; re-entering the cortex the tube again becomes convoluted, until it joins one of the straight tubes in the medullary ray; from this point onwards the tubes run straight down the medullary ray and pyramid, joining tube with tube, until they terminate by orifices on the papilla. The epithelium lining this tract is distinguishable into three varieties. 1. Squamous epithelium lining the capsule. 2. A more or less granular and striated granular epithelium lining the convoluted portions in the cortex, and the ascending limb of the loop in the boundary zone. 3. A clear cubical lining epithelium in the descending limb of the loop, and in the straight tubes running in the medullary ray and in the pyramid. Of these three epithelia the second is of most physiological importance; its individual cells are active masses of protoplasm concerned in extracting from the blood the chief organic constituents of the urine, and, upon occasion, certain foreign materials experimentally injected.

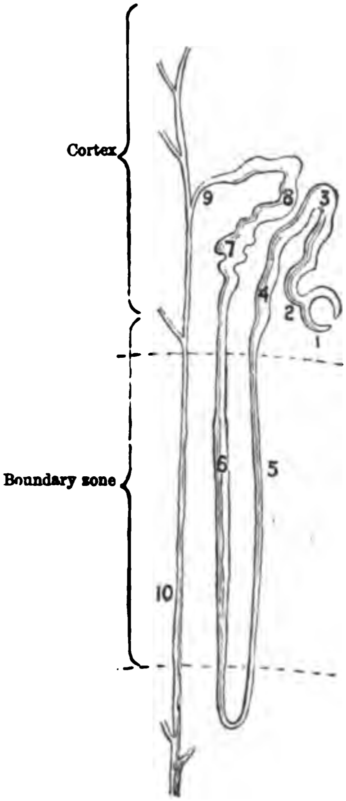


FIG. 86.—COURSE OF A URINARY TUBULE.

1. Capsule of Bowman
2. Neck
3. First convoluted tube
4. Spiral tube
5. Descending limb of loop of Henle
6. Ascending limb of loop of Henle
7. Irregular tube
8. Second convoluted tube
9. Junctional tube
10. Collecting tube

The urine.—The urine is continuously secreted by the kidneys and passed along the ureters to the bladder, where it accumulates, and from which it is discharged at intervals by the act of micturition. The average amount of urine secreted per diem is 1,500 c.c. or about 50 oz., and the capacity of the bladder is about 500 c.c.

Composition of the urine.—Fresh normal urine is a clear yellow fluid of acid reaction with a specific gravity of 1015 to 1025, being a solution in water of *urea* and *salts*, viz. about 2 per cent. of urea and 1½ per cent. of salts. Stated more in detail, the composition of urine as regards its most important constituents, and the average daily discharge of such constituents, are as follows:—

	per 1,000		per diem	
Water	960		1,450	c. cm.
Urea	20		30	grammes
Uric acid	2		0·75	„
Hippuric acid			0·75	„
Creatinin			1·5	„
Phosphates	15	H_3PO_4	3	„
Chlorides		HCl	7·5	„
Sulphates		H_2SO_4	3	„
&c., *e.g.* mucus & extractives	3			

The *acidity* of urine is not due to the presence of any free acid; methyl orange, which is reddened by free acid, is not affected by urine; sodium hyposulphite, which gives a precipitate of sulphur with free acid, gives none with urine. The acidity is attributable to the presence of acid sodium phosphate, NaH_2PO_4, and of free carbonic acid gas. Normally the acidity of fresh urine increases a little at first, it subsequently diminishes and is replaced by alkalinity, this last change being due to a fermentation in the course of which urea is converted into ammonium carbonate. The normal acidity of urine is equivalent to that of a 1 per 1,000 solution of H_2SO_4. The acidity is somewhat more pronounced in the urine passed in the morning, less so in that passed after a meal, and it varies greatly with the nature of the diet; the urine of herbivorous animals and of vegetarians is alkaline and turbid, that of carnivorous animals and of ordinary men is acid and clear, that of herbivorous animals during starvation—when they are practically carnivorous of their own flesh—is also acid and clear. Abnormally the urine may become excessively acid or alkaline. In the first case, a 'cayenne pepper' deposit of uric acid (visible to the naked eye), and 'envelope crystals' of oxalate of lime, are discoverable by the microscope in the urine which has been allowed to stand. The second state may be due to disease of the kidney or bladder, causing the urine to decompose before it is discharged, or it may be caused by nothing more serious than an excessive consumption of fruit or vegetables; 'knife-rester' crystals of 'triple phosphate' ($Mg.NH_4 PO_4$) and 'hedgehog crystals' of ammonium urate are apt to form in such urine.

A normal clear urine may become turbid on cooling, in consequence of the deposition of urates; on the other hand, a normal urine may become turbid on heating, in consequence of the deposit of phosphates; in the first case the turbidity is removed by heating, in the second case it is removed by acetic or nitric acid.

The *specific gravity*—1015 to 1025—varies with the amount of urine passed; this again varies with the amount of water discharged from the lungs and skin. Thus in winter the urine i dilute, pale, and copious, as compared with the summer urine which is concentrated, dark, and scanty. Normally, the tota amount of solids per 1,000 contained in a sample of urine i approximately indicated by multiplying the last two figures o the specific gravity by 2·2; *e.g.* with S.G. 1015 the total solid per 1,000 are 33; with S.G. 1020 the total solids per 1,00 are 44.

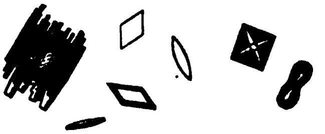


FIG. 87.—CRYSTALS IN ACID URINE; URIC ACID AND OXALATE OF LIME.

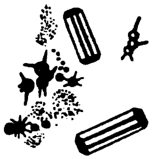


FIG. 88.—CRYSTALS IN ALKALINE URINE: TRIPLE PHOSPHATE AND AMMONIUM URATE

The *colour* of the urine is due to the presence of urobili which, as indicated by its name, is a derivative of bile-pigment urobilin is in fact identical with hydrobilirubin.

Mechanism of secretion; theories.—The secretion of urine i an active process, not a passive filtration. On the passive filtr tion theory (Ludwig, 1844 to 1870), it was supposed that th entire urine is filtered under pressure from the blood in a ver dilute state at the glomeruli, and that it gradually becomes mo and more concentrated by reabsorption of water as it pass along the tubules. On the active secretion theory (Bowman 1842, Heidenhain 1875), it is supposed that the epithelial cells lining the glomeruli and the convoluted tubules, separate the water, urea, and other urinary constituents from the blood, and that different shares of work belong to the two classes of cells—water being separated by the cells of the glomeruli; urea, uric acid, &c., by the cells of the convoluted tubes and of the ascending limb of Henle's loop. The anatomical disposition of the renal vessels is such as to suggest filtration under high pressure at the glomeruli, secretion under low pressure by the convoluted tubules, and in favour of the filtration theory we have also the fact that, as a rule, the amount of urine is greater and smaller as blood-pressure rises and falls. But, as we shall see, there are exceptions to the rule, and the facts can be otherwise explained. The active secretion theory is upheld by the manner in which the secretion of indigo carmine (=sodium sulphindigotate) has been traced by Heidenhain, and is supported by Nüssbaum's experiments on the kidneys of amphibia; the theory is not contradicted by any of the facts advanced in support of the pressure theory.

Moreover, a simple comparison of the percentages of substances contained in the blood and in the urine respectively is highly suggestive of separative activity rather than of passive filtration; the normal percentage of urea is 2 per cent. in urine and only ·02 per cent. in normal blood, and not above ·2 per cent. in extreme uræmia; in diabetes the percentage of sugar in the urine has been found more than ten times that in the blood.

Heidenhain's experiments with indigo carmine are as follows:—The spinal cord or bulb of a rabbit is divided in order to lower the blood-pressure, indigo carmine (5 to 20 c.c. of a saturated solution) is injected, the animal is killed ten minutes to an hour later, its kidneys are removed and injected with alcohol. On slicing open the kidney, which has become blue, the coloration is seen in a well-marked band which occupies the whole breadth of the cortex, and sometimes in a fainter band corresponding with the boundary zone; on microscopic examination the coloration is found to be due to blue granules in or between the epithelial cells, (1) of the convoluted tubes, (2) of the ascending limb of Henle's loop, and (3) in the lumen of the tubes themselves; the capsules of the glomeruli are found to be quite free from blue granules. This typical experiment is accepted as an illustration by means of a visible substance of what probably is the mode of separation of the invisible substance urea. The division of the spinal cord has prevented any copious stream of water from flowing through the glomeruli, and the blue granules have remained in or near the parts engaged in their separation.

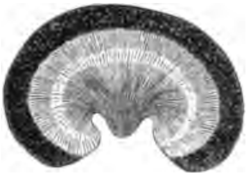


FIG. 89.—RABBIT'S KIDNEY.

One hour after division of spinal cord, and injection of 5 c.c. sulphindigotate of soda. (Heidenhain.)

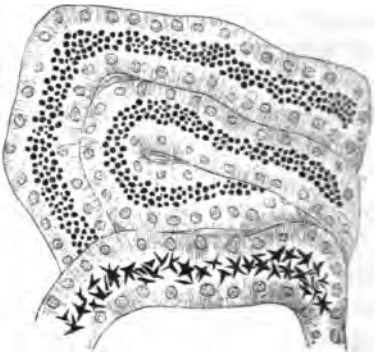


FIG. 90.—MICROSCOPIC APPEARANCE OF CONVOLUTED TUBULES. (Heidenhain.)

Various modifications of the above typical experiment are taken to be confirmatory of this interpretation. The indigo injection has been made without previous division of the spinal cord, and the blue granules have been found massed in the pyramids or in the pelvis, as if they had been washed onwards by the water stream. This last experiment has been repeated with previous corrosion of a superficial portion of cortex by silver nitrate, so as to interfere with the action of the subjacent glomeruli, and the wedge of kidney below the cauterised surface has been found with blue zones as if unwashed, contrasting with adjacent parts in which the water current had proceeded unchecked. These results are consonant with—if they do not conclusively prove—the view that water is secreted by the glomeruli, urea (as represented by indigo carmine) by the tubuli contorti.

In prosecution of these inquiries, Nüssbaum utilised the amphibian kidney, which presents certain advantages for experimental purposes, by virtue of its double blood-supply from the renal artery and from the renal portal vein—the artery mainly supplying the glomeruli, the vein mainly supplying the tubuli Nüssbaum's most pertinent observation was to the effect that the sulphindigotate is discoverable in the tubuli after ligature of the renal artery; he did not, however, perform the counter experiment of ligature of the vein. He found that albumin, sugar, carmine, do not pass into the urine after ligature of the renal artery, and concluded that these substances were secreted by the glomeruli. He also found, however, that by injecting urea he could get secretion of water containing urea, even after ligature of the renal artery. This contribution of Nüssbaum's gives very little direct support to the theory of Heidenhain, and the method is open to the objection that ligature of the renal artery does *not* arrest circulation through the glomeruli (Adami).

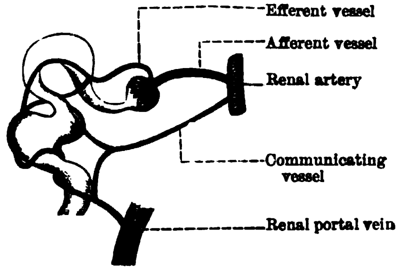


FIG. 91.—DIAGRAM TO ILLUSTRATE THE DOUBLE BLOOD-SUPPLY OF THE NEWT'S KIDNEY. (After Nüssbaum.)

The renal artery forms the glomeruli; the renal portal vein supplies the capillaries of the tubules.

The two systems of capillaries are not completely distinct; the connection is such that while the glomeruli are exclusively supplied by the renal artery, the tubules are supplied chiefly by the renal portal vein, but also to some extent by the renal artery.

Effects of blood-pressure.—The secretion of urine rises and falls with rising and falling blood-pressure; clinically, in cases of heart-disease, a falling off in the amount of urine gives warning that the circulation is failing. But that the secretion is not a simple consequence of the pressure of the blood in the renal vessels, is shown by the effect of compressing the renal vein, which, while not lowering the pressure, arrests the secretion. A more correct and comprehensive general statement is that the secretion of urine increases and diminishes with increased and diminished *blood-flow*. A justification of this statement is to be found in the subjoined table, which summarises the effects of various kinds of experiments upon the blood-pressure in the renal vessels, upon the blood-flow through the kidney, and upon the amount of urine secreted. More or less urine is given out according as more or less blood comes under the influence of the secreting cell, and if rising and falling blood-pressure produce as a rule more or less secretion, it is because rising and falling blood-pressure generally entail increased and diminished blood-flow.

	Renal blood-pressure	Renal blood-flow	Secretion of urine
Destruction of spinal bulb . . .	*dimin.*	*dimin.*	*dimin.*
Excitation „ . . .	*incr.*	*dimin.*	*dimin.*
Section of renal nerves . . .	—	*incr.*	*incr.*
Excitation „ „ . . .	—	*dimin.*	*dimin.*
Excitation of spinal bulb after section of renal nerves . . .	*incr.*	*incr.*	*incr.*
Compression of renal artery . .	*dimin.*	*dimin.*	*dimin.*
„ „ renal vein . . .	*incr.*	*dimin.*	*dimin.*
Failure of heart	*dimin.*	*dimin.*	*dimin.*
Digitalis	*incr.*	*incr.*	*incr.*

These several effects are the simple physical consequenc of varying vaso-constriction throughout the system and in tl kidney. It is hardly necessary to explain them at length; tl facts are stated in the table in their simplest form. Destructi of the bulb relaxes the vessels all over the body, inclusive the kidney, and the circulation is everywhere more sluggis Excitation of the bulb constricts the vessels all over the bod inclusive of the kidney, and although pressure is raised, le blood gets through the constricted vessels of the kidney; however, these vessels be cut off from vasomotor action by secti of the renal nerves, then excitation of the bulb has the effe of sending a larger amount of blood through the kidney.

The method by which the circulation of the kidney can most directly studied is to observe the alterations of volu which the organ undergoes. An instrument devised by Roy f this purpose, termed the oncograph, has already been describ (p. 77). It consists of two parts united by a tube, one t exploring chamber or 'oncometer,' which receives the kidney, t other the recording chamber or 'oncograph' proper, whi carries a recording lever fixed to a piston. The apparatus bei filled with oil, any swelling or shrinking of the kidney causes t piston to rise or fall. Variations of blood-pressure cause cor sponding variations of volume; the first column of the tab therefore, holds good for the alterations of volume produced various experiments; *i.e.* the kidney shrinks with vaso-constr tion (rise of pressure), swells with vaso-dilatation (fall of pr sure); if, however, its nerves are divided, then it swells with r of pressure and shrinks with fall of pressure. In reasoning o the connection between pressure and volume, it is to be reme bered that the renal arteries share in the general contraction which causes rise of pressure, therefore the kidney shrinks with rise of pressure by vaso-constriction, but that they are also dilatable; therefore, unless the kidney shrinks by vaso-constriction, it passively swells from any increase of pressure, *e.g.* by respiratory undulations of pressure, or by excitation of the bulb after section of renal nerves. The only case in which there is anything to add is that of section and excitation of the renal nerves, of which we could not definitely state the effects on renal pressure, but which very obviously produce—the first, a dilatation, the second, a contraction of kidney volume.

We may take this occasion to define the physiological character of the renal nerves. Experiments by section and excitation demonstrate clearly the existence of vaso-constrictor action, less clearly that of vaso-dilatator action, not at all that of secreto-motor action. That constricting fibres exist in the renal nerves is shown by expansion of the kidney after the nerves are cut, and by the contraction of the kidney which is the usual result of their excitation; that dilating fibres also exist in the renal nerves is shown by the expansion of the kidney which is the occasional effect, or after-effect, of such excitation (Bradford), but as in other nerves the dilating are ordinarily masked by constricting effects. Renal nerve fibres (in the dog) leave the spinal cord by the anterior roots from sixth thoracic to second lumbar, in greatest abundance by the last three or four thoracics.

Origin and separation of urea.—The physiological history of urea as known to us at the present day, may be summed up as follows:—*Urea is the chief product of the disintegration of proteid food; it is formed in the tissues; it is discharged into the blood; it is separated from the blood by the action of the renal epithelium; it is expelled in the urine.* The first of these propositions is proved by the series of experiments in course of which the old view, that urea is the measure of muscular waste, was disproved, and replaced by the modern view that urea discharged is in proportion with proteid food consumed. These observations, as the outcome of which the doctrine of nitrogenous equilibrium was formulated, will be considered in Chapter VII., and we shall at this stage confine ourselves to the recognition of the fact that urea is mainly derived from proteid which has not actually become protoplasm, but which has become disintegrated under the influence of protoplasm. The simplest and most cogent proof of the second proposition, viz. that urea is formed by the tissues, is furnished by the fact that urea continues to be formed and accumulates in the blood (uræmia) when renal secretion has been abolished by removal of the kidneys, or by disease, and we shall see later that the liver is to be recognised as the most prominent among urea-making tissues (p. 244). The production of uræmia also forms part of the proof of the third proposition, viz. that urea is separated by the kidney, but the specific proof of the separative activity of renal epithelium is afforded by Heidenhain's observations of the excretion of indigo carmine and of uric acid. The fourth proposition needs no formally stated proof; we know that urea is contained in the urine.

Urea is the chief normal constituent of urine, and the vehicle in which nitrogen is discharged from the body. It is a crystalline body soluble in water and in alcohol, capable of forming compounds with nitric acid (nitrate of urea), with oxalic acid (oxalate of urea), and wit mercuric nitrate, and of being decomposed by fermentation and b solutions of the hypobromites or hypochlorites. Urea has the empiric formula CON_2H_4, its molecular weight is 12+16+28+4 or 60, o which nitrogen constitutes 28 parts, or nearly one half. Thus 6 grammes of urea will yield 28 grammes or 22·38 litres of nitrogen 1 gramme of urea in urine should yield 373 c.c of nitrogen at normal temperature and pressure, but is actually found to yield only 354 c.c so that 1 c.c. N represents $\frac{1}{354}$ gramme urea. The rational formul of urea is $CO.2(NH_2)$, and exhibits it as the diamide of carboxy It is isomeric with ammonium cyanate $NH_4\text{-}O\text{-}CN$, and as a fir stage in its alkaline fermentation yields ammonium carbonat $\underset{\text{urea}}{CO(NH_2)_2}+\underset{\text{water}}{H_2O}=\underset{\text{ammonium carbonate}}{(NH_4)_2CO_3}$. By further fermentation it decom poses into CO_2 and N, and the same result is obtained in consequen of decomposition by chemical re-agents; facts which furnish mean for estimating a *quantity* of urea by a *volume* of nitrogen evolved.

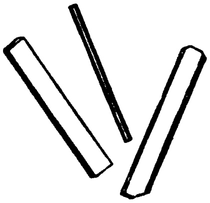


FIG. 92.—UREA. (From Funke's Atlas.)

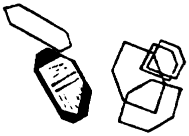
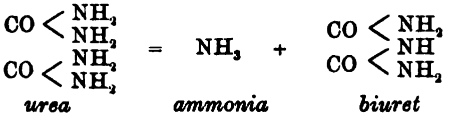


FIG. 93.—NITRATE AND OXALATE OF URE

Crystals of urea, heated in a dry test-tube to 150–160°, melt an give off ammonia; the residue is biuret, which if dissolved in water an tested by a trace of $CuSO_4$ and excess KHO, exhibits a violet colour; if heated above 170° either urea or biuret yield ammonia and cyanuric acid.



$$\begin{matrix} CO < {NH_2 \atop NH_2} \\ CO < {NH_2 \atop NH_2} \end{matrix} = NH_3 + \begin{matrix} CO < {NH_2 \atop NH} \\ CO < NH_2 \end{matrix}$$

urea *ammonia* *biuret*

$$3CO(NH_2)_2 = 3NH_3 + C_3H_3N_3O_3$$

urea *ammonia* *cyanuric acid*

Synthesis of urea.—Chemically as well as physiologically urea is of great importance as being the first animal product which has been reproduced by synthesis from inorganic bodies, or from the elements themselves, without the intervention of animals. Nitrogen passed through a tube containing carbon and potassium carbonate heated to redness gives potassium cyanide; $K_2CO_3+N_2+2C_2=KCN+3CO$; by oxidation the cyanide gives cyanate; potassium cyanate with ammonium sulphate gives potassium sulphate and ammonium cyanate; $2KCNO+(NH_4)_2SO_4=K_2SO_4+2NH_4CNO$; evaporation of ammonium cyanate yields urea.

Preparation of urea from urine.—Evaporate one or two litres of urine on a water-bath to a small bulk. Add nitric acid to form nitrate of urea. Pour off the fluid, and mix the crystalline mass with barium carbonate. Extract the mixture with alcohol. Filter, evaporate, and dry the crystalline residue of urea. Purify by recrystallisation.

The *presence of urea* is recognised in a fluid by the crystals of nitrate of urea which are formed when a drop of the fluid to which nitric acid has been added is allowed to evaporate on a slide and examined by the microscope. Nitrate of urea appears in the form of six-sided rhombic tables. The presence of urea may be suspected in a fluid which gives out bubbles on the addition of hypobromite of soda.

The *quantity of urea* in a fluid known to contain urea, *i.e.* in urine, is most conveniently and rapidly ascertained by the hypobromite method (Knop-Hüfner). It should first be remarked that an estimation of urea in a single sample of urine is of little value; the estimation, to be of any use, must be taken with a sample of the entire urine collected during 24 hours, so that the total discharge of urea from day to day can be calculated. The hypobromite method is easy and expeditious, and therefore suitable for clinical use (fig. 94). For more exact determinations, the distillation method in one or other of its numerous modifications must be adopted; it is more laborious, but of more general application, and by it the amount of nitrogen present in any nitrogenous substance—solid or liquid—can be determined (fig. 95).

Uric acid, which is present to a very small amount in urine (the total excretion not exceeding ½ gramme per diem), is from a pathological standpoint its most important constituent. An excess of uric acid in the system is the chief physical token of gout, and the common material of 'gravel,' and of 'calculus,' and of 'chalk stones.' Normally, uric acid exists in the urine in combination with potassium and sodium as urates of these metals, and, unless the urine be of excessive acidity, it does not crystallise out. But in an unusually acid urine, or in a urine which has been acidified, crystals of uric acid form after a time, which from their appearance, have been compared with cayenne pepper; they are diamond-shaped, and their colour is due to the urinary pigments.

Uric acid is insoluble in alcohol, and scarcely soluble in water or in acid solutions, readily soluble in alkaline solutions. The first indication to be fulfilled in cases of gout or gravel is therefore to render th urine alkaline. In birds and snakes uric acid is the chief vehicle nitrogenous excretion; the excrement of snakes, for example, bein little else but uric acid, and having on that account considerabl commercial value as a source of uric acid. In mammalia uric acid i a variable product, in herbivora it is replaced by hippuric acid, in th dog by cyanuric acid. Uric acid is a less oxidised product than ure as may be recognised in the empirical formulæ of the two bodies—ure CON_2H_4, uric acid, $C_5O_3N_4H_4$; it is easily oxidised, and can there fore act as a deoxidising or reducing agent, *e.g.* on silver nitrate and o

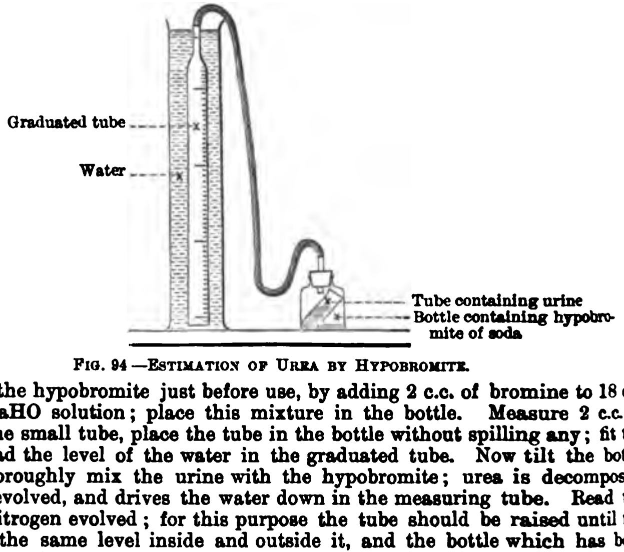


FIG. 94—ESTIMATION OF UREA BY HYPOBROMITE.

Prepare the hypobromite just before use, by adding 2 c.c. of bromine to 18 c.c of strong NaHO solution; place this mixture in the bottle. Measure 2 c.c. o urine into the small tube, place the tube in the bottle without spilling any; fit th cork and read the level of the water in the graduated tube. Now tilt the bott so as to thoroughly mix the urine with the hypobromite; urea is decomposed nitrogen is evolved, and drives the water down in the measuring tube. Read th volume of nitrogen evolved; for this purpose the tube should be raised until th water is at the same level inside and outside it, and the bottle which has bee heated by chemical action should be cooled. Let us say that the volume o nitrogen evolved by 2 c.c. of urine measures 18 c.c., and that the day's urin amounted to 1,500 c.c. If 2 c.c. yields 18 c.c. nitrogen, 100 c.c. would yield 900 c. nitrogen, representing $\frac{900}{354}$ grammes urea, *i.e.* 2·54 grammes, and the 1,500 c. contained 38 grammes urea. The formula setting forth the decomposition of ure by the hypobromite as above is $CON_2H_4 + 3NaBrO = 3NaBr + 2H_2O + CO_2 + N_2$; th CO_2 is absorbed by the excess of NaHO, and the only gas in the measuring tube is copper sulphate. The action on silver nitrate is utilised as a rough test—uric acid solution dropped on a filter paper, moistened with $AgNO_3$, gives a black or brown stain of reduced silver (Schiff.). The

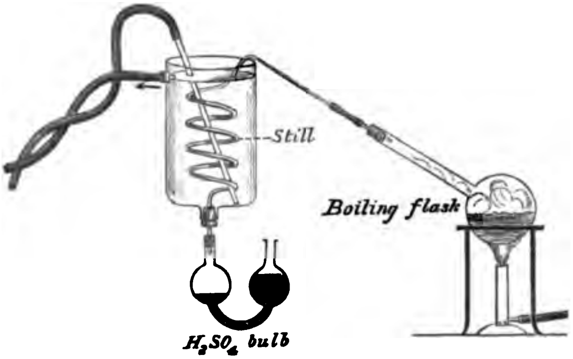


FIG. 95.—ESTIMATION OF NITROGEN BY DISTILLATION OF AMMONIA INTO SULPHURIC ACID. KJELDAHL METHOD; WILFARTH MODIFICATION. (Argutinsky.)

Principle.—The proteid is oxidised by heating with strong H_2SO_4, ammonium sulphate is formed; the fluid is rendered alkaline and heated, ammonia is driven off, and estimated by the loss of acidity in a titrated solution of H_2SO_4.

First step. Oxidation.—Boil with 25 c.c. of the following mixture (5 parts H_2SO_4, 1 part H_3PO_4), to which is added $\frac{1}{10}$ c.c. Hg, in a long-necked flask of about 200 c.c. capacity, until the fluid is decolorised. For urine half an hour's boiling will suffice, for meat two hours will be required. Cool, and dilute with distilled water to about 150 c.c.

Second step. Distillation.—Transfer the diluted fluid to a larger long-necked flask (about a litre capacity). Add alkali in not too large excess, and some talc to obviate bumping. Add 12 c.c. of strong K_2S solution (2 parts salt in 3 parts water). Connect with the spiral glass still and sulphuric acid bulb as in diagram: capacity of each bulb to be about 200 c.c.; amount of decinormal H_2SO_4 to be 50 c.c. Boil for three quarters of an hour, disconnect the flask from the still. Care must be observed at the commencement to quickly connect still with distilling flask after adding alkali; the amount to be added should, therefore, be ascertained by a preliminary trial.

Third step. Titration.—Use a decinormal solution of KHO, and methyl orange as the indicator.

Apparatus and reagents to be prepared.—Decinormal solutions of H_2SO_4 (4·9 grms. in 1,000 water); of KHO (5·6 grms. in 1,000); of Na_2CO_3 (5·3 grms. in 1,000). Strong H_2SO_4. Strong H_3PO_4. K_2S solution (2 in 3). KHO (S. G. 1·25). Mercury. Talc. Methyl orange. Distilled water. 200 c.c. flask. 1,000 c.c. flask. Still. H_2SO_4 bulb. Burettes and beakers.

Verify the decinormal acid and alkali before use with decinormal sodium carbonate as the starting point. Test the method with ·1 gramme of urea, which should yield ·046 gramme N, *i.e.* a loss of acidity = 33 c.c. decinormal acid or alkali. Expect from 1 gramme of ordinary meat a loss of acidity = about 25 c.c. of decinormal H_2SO_4 or KHO = ·035 gramme N; from 5 c.c. urine, a loss of acidity = 35 c.c. of standard solutions = ·05 gramme N. ($N : H_2SO_4 = 2 : 7$.)

action on copper sulphate should be remembered as a possible source of confusion between sugar and uric acid.

Preparation of uric acid from serpent's excrement. Dissolve the excrement in weak NaHO by the aid of heat. Precipitate uric acid from the hot solution with hot HCl. Wash with water, and dry.

Detection of uric acid in the blood, and in pathological fluids. A few drops of blood-serum or other fluid, acidulated, and allowed to evaporate in a watch-glass, in which a linen fibre is laid, deposits crystals of uric acid on the fibre, recognisable by the microscope. This is applicable to fluids taken from gouty subjects. By the above method the presence of uric acid in the urine may be conveniently demonstrated.

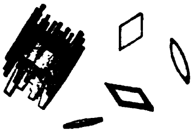


FIG. 96.—URIC ACID CRYSTALS.

Murexide test.—Uric acid cautiously evaporated with HNO_3 gives a yellow stain, which turns purple with NH_3, violet with KHO.

Quantitation of uric acid in the urine.—The clinical significance of uric acid is such as to render an accurate and expeditious method most desirable. No such method exists. After the trial of several, we shall revert to that of Heintz, which, although not to be relied on, is simple and expeditious, and has usually been adopted for clinical purposes. It is as follows :—100 c.c. of urine are acidified by 5 c.c. HCl, and set aside for twenty-four to forty-eight hours ; the crystalline deposit of uric acid is collected on a weighed filter, washed, dried, and weighed.

Hippuric acid, $C_9O_3H_7N$, as indicated by its empirical formula, is still less oxidised than uric acid ; it is present in considerable quantity in the urine of cattle, is also present in normal human urine, and may be temporarily increased by the administration of benzoic acid. Benzoic acid and glycin form glycobenzoic or hippuric acid, as cholalic acid and glycin form glycocholic acid. Hippuric acid is a crystalline body, soluble in alcohol, and hardly soluble in water ; heated in a dry tube it sublimes and deposits benzoic acid, which is also recognisable by its characteristic smell.

Preparation of hippuric acid from cow's or horse's urine.—Mix with milk of lime, filter, evaporate—add HCl—wash and dry the crystals—redissolve in boiling water—recrystallise.

From human urine.—Swallow 1 gramme benzoic acid in a gelatin capsule—collect the urine of the succeeding four hours—proceed as above.

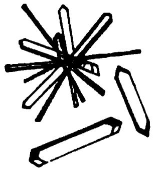


FIG. 97.—HIPPURIC ACID. (From Funke's Atlas.)

FIG. 98.—CREATININ-ZINC-CHLORIDE.

Creatinin, $C_4OH_7N_3$, present in the urine, is derived from creatin present in muscle and in blood ; it is a still less oxidised product than either uric or hippuric acids. Its presence is recognisable by the following test :—Add sodium nitro-prusside, heat and add NaHO, the solution is ruby-red, soon becoming yellow, and turning green or blue on addition of acetic acid.

Quantitation of creatinin. (Neubauer.)—250 c.c. of urine are treated with milk of lime until the reaction is alkaline, then with $CaCl_2$ until no further precipitate appears. The filtrate is evaporated on a water-bath to a syrupy consistence, and extracted for several hours with strong alcohol. To the alcoholic extract are added a few drops of a neutral alcoholic solution of $ZnCl_2$, and the beaker is set aside for three days in a cool place. A crystalline precipitate of creatinin-zinc-chloride, in the form of rosettes, visible to the naked eye, is found at the bottom and sides of the beaker. This ppt. is collected on a weighed filter, which is subsequently dried and weighed. Expect an increase of about ·4 gr., *i.e.* ·25 gr. creatinin; $\frac{\text{creatinin}}{\text{creatinin-zinc-chloride}} = {\cdot}624$. Examine some of the deposit with the microscope.

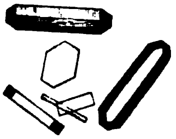


FIG. 99.—CREATIN. (From Funke's Atlas.)

The bodies above considered—urea, uric acid, hippuric acid, and creatinin—are the chief nitrogenous derivatives present in normal urine; urea is the most fully oxidised, creatinin the least fully oxidised; uric acid occupies an intermediate position. A further indication of the relationship between these several bodies is furnished by the fact that urea can be obtained from uric acid by oxidation, and from creatin by treatment with alkalies.

Inorganic salts.—The chief inorganic salts of the urine are *chlorides*, *phosphates*, and *sulphates*. Of these the sulphates are of most physiological interest, for they represent the form in which nine-tenths of the sulphur contained in proteid food escapes from the body; they are not simply reappearing sulphates swallowed with food, for the amount of food sulphates is so small as to be negligible. Chlorides and phosphates on the other hand proceed from chlorides and phosphates swallowed with the food. The notion that the amount of phosphate excreted varies with the degree of mental exertion is entirely unsupported by facts, and when we realise that the amount of phosphoric acid in the whole cerebro-spinal substance is only $\frac{1}{10}$ the amount in the muscles, and $\frac{1}{100}$ the amount in the bones, there is no ground for expecting to find variations of nerve metabolism represented by variations of phosphoric acid in the urine. The average daily excretion of the three acids in the form of salts is HCl, 7·5 grms.; H_3PO_4, 3 grms.; H_2SO_4, 3 grms. The excretion of chlorides is said to be diminished in pneumonia; that of phosphates is said to be increased in fever and in bone disease, diminished during pregnancy.

Chlorides (Na and K).—The presence of chlorides is recognised by the precipitate formed with silver nitrate, insoluble in nitric acid.

Quantitation (Mohr).—The principle of the method is as follows:—Chlorides are precipitated by a standard solution of silver nitrate

(29·075 grms. in 1,000), of which 1 c.c. will precipitate ·01 grm. NaCl; potassium chromate is used to indicate when an excess of silver has been reached. Take 10 c.c. of urine and dilute ten times with distilled water, add a few drops of potassium chromate solution; run the silver solution into this mixture until an orange colour appears, showing that the excess point has been passed. If, for instance, this is the case when 6 c.c. of silver solution have been added, the 10 c.c. of urine are calculated as containing ·05 grm. NaCl, or ·5 per 100. The method is expeditious, and therefore suitable for clinical work, but it is not very exact; the readings are generally 1 c.c. too high, and should be corrected by that amount.

Phosphates (Mg, Ca, Na, K).—The addition of ammonia to urine gives a ppt. of earthy phosphates (Ca and Mg), the filtrate from this, or the original urine, gives a ppt. of alkaline phosphates (Na and K) on boiling with ammonium molybdate and nitric acid.

The amount of phosphoric acid present is determined as follows:—

Two solutions are prepared. (1) *Standard uranium acetate solution*, 35 grm. to 1,000 c.c. water with 25 c.c. glacial acetic acid. 1 c.c. of this solution is nearly equivalent to ·005 grm. P_2O_5. (2) A fresh 10 per 100 solution of potassium ferrocyanide to be used as the *indicator*.

Heat 50 c.c. of urine with successive additions of the standard solution from a graduated pipette, until a drop of the mixture strikes brown with a drop of the indicator; *e.g.* if the brown colour is obtained after 20 c.c. of the standard solution have been added, the 50 c.c. urine contain ·100 grm. P_2O_5, *i.e.* ·2 per 100. The uranium solution should be previously adjusted so that 20 c.c. will exactly balance 50 c.c. of a ·2 per cent. P_2O_5 solution (ammonio-sodic phosphate 5·886 grm. in 1,000 water).

The principle upon which the determination depends is that uranium nitrate combines with phosphoric acid in a definite ratio, the point of excess being indicated by the brown colour which *free* uranium nitrate gives with potassium ferrocyanide.

Sulphates.—Sulphur (mainly derived from proteid) escapes in the urine in the form of sulphates:—(1) In chief part as inorganic sulphates (of K and Na). (2) In small part as aromatic sulphates, viz. an indigo-yielding salt, potassium indoxyl sulphate, $C_8H_6NKSO_4$; and a phenol-yielding salt, potassium phenyl sulphate, $C_6H_5KSO_4$.

Under normal circumstances the amount of aromatic sulphates present in the urine is about $\frac{1}{10}$ that of the inorganic sulphates, but abnormally, when putrefaction of proteid occurs in the small intestine, leading to the formation of aromatic bodies such as indol and phenol, this proportion may be considerably increased. The total amount of sulphates depends upon the amount of proteid consumed; the average daily excretion of 3 grms. H_2SO_4 contains about 1 grm. S, *i.e.* about as much as is contained in 100 grms. of proteid.

The *presence* of sulphates is recognised by the precipitate formed with barium chloride, insoluble in hydrochloric acid. The indigo-yielding substance (so-called 'indican') is present in excess if the urine on boiling with HCl gives a pink colour. Its physiological antecedent is indol, formed in the intestine by the putrefaction of proteids. To demonstrate its presence in ordinary urine, a considerable quantity, *e.g.* 500 c.c., should be taken, and to it 250 c.c. pure HCl be added. A coppery scum forms on the surface. The greater part of the fluid is syphoned off, and the remainder, including the scum, is thrown on a filter. The filter is washed with ammonia, and then with alcohol. The alcohol takes up indigo and becomes red; on boiling it becomes blue.

To estimate the *total amount* of sulphates (inorganic and aromatic), add 5 c.c. HCl to 100 c.c. urine, and heat in order to break up aromatic sulphates; precipitate with $BaCl_2$, and heat on water-bath; filter, wash with water and with alcohol, dry and weigh. Supposing the filter to have gained ·5 grm. in weight by the $BaSO_4$ ppt., we ascertain by calculation that the amount of H_2SO_4 present is ·21 grm., and of S about ·07 grm. To estimate the amount of aromatic sulphates alone, the same process is gone through with the *filtrate* of urine from which the inorganic sulphates have been removed by baryta mixture (BaO and $BaCl_2$), without previous heating with HCl. The weight of the $BaSO_4$ ppt. is more exactly obtained by igniting the filter paper and ppt. in a covered platinum capsule, and after cooling in an exsiccator, weighing the ash in the capsule; the weight of the capsule and that of the filter paper ash are known, the remainder is the weight of $BaSO_4$ (Salkowski).

A more expeditious method is by volumetric determination of the amount of $BaCl_2$ required to precipitate all the sulphates present. Each c.c. of the standard barium solution (30·5 grm. $BaCl_2$ in 1,000) will precipitate ·01 grm. SO_3 as $BaSO_4$. The excess point is indicated by the aid of a 20% solution of potassium sulphate; a drop of this solution mixed with a drop of the clear stratum of the urine under treatment should give no more than a slight cloudiness; if a clear drop of the latter, mixed with a drop of $BaCl_2$ solution, gives a precipitate, the process is not yet complete; if it becomes milky with a drop of the indicator, too much $BaCl_2$ has been added. The urine is to be heated before each addition of $BaCl_2$. If it has been previously boiled with HCl, the total sulphates are determined; if not so treated, only the inorganic sulphates. Supposing the excess point to be obtained with 15 c.c. of barium solution added to 100 c.c. urine, the percentage of SO_3 is known to be ·15 (= nearly ·2 H_2SO_4).

Abnormal constituents.—The substances which most commonly appear in the urine under abnormal circumstances are *albumin*, *blood*, and *sugar*; and the part of the kidney by which they are believed to escape is the glomerulus. In jaundice the urine is tinged with *bile-pigment.*

Albumin may leak from the blood into the urine under several conditions and in several forms. It may appear as serum-albumin, serum-globulin, albumose, or peptone. Its presence may be due to serious structural alteration of the kidney, as in Bright's disease, or to a trifling and evanescent alteration of function, as by diet, or in a condition of fatigue, and experimentally it may be induced by altering the state of the blood, or by interfering with the circulation of the kidney. The readiest and most certain test for albumin in the urine is heat '*plus*' nitric or acetic acid. If the acidulated urine becomes turbid, or coagulates on boiling, it contains albumin. The degree of the turbidity or the amount of the coagulation gives a measure, though a very imperfect one, of the amount of albumin. To make a correct estimate the acidified boiled urine should be thrown on a weighed filter, which is subsequently dried and weighed.

The non-escape of albumin under normal conditions is to be ascribed to the integrity of the glomerular epithelium, and to a normal state of the blood. Interference with the nutrition of the kidney as by temporary arrest of its circulation, alteration of the composition of the blood as by injection of water or of lake blood, are apt to provoke albuminuria or even hæmoglobinuria.

Sugar.—The *presence* of sugar is readily ascertained by Trommer's test. A urine which contains sugar gives a red or yellow precipitate on boiling with caustic potash and a few drops of copper sulphate; a preferable mode of testing is to add urine to Fehling's fluid which has just been boiled, heating the mixture again to near boiling point. The *amount* of sugar present may be determined in several ways, of which the following are the principal:—(1) by *Fehling's solution*, (2) by *fermentation*, (3) by the *polarimeter*. Of these methods the most exact as well as the most delicate is the first, which is as follows:—Fehling's solution[1] is prepared of such strength that the copper salt in 10 c.c. is reducible by $\frac{1}{20}$ grm. sugar; the completion of reduction is indicated by disappearance of the blue colour of the solution. A measured quantity of Fehling's solution, say 10 c.c., or 1 c.c., diluted five times, is boiled in a capsule or test-tube with urine, which is added until the blue colour disappears, the quantity of urine added is therefore known to contain $\frac{1}{20}$ or $\frac{1}{200}$ grm. glucose. For clinical use the determination can be conveniently carried out in a test-tube with 1 c.c. of Fehling, and it will usually be necessary to dilute the urine; for more exact determi nations 10 c.c. should be employed, and the boiling carried on in a capsule into which the urine is dropped from a burette. If, for instance, 1 c.c. is decolorised by 4 c.c. of a urine which has been diluted ten times, the original urine is known to contain 1·25 per cent. of sugar; if the day's urine amounted to 3,000 c.c., then the sugar passed in that day would amount to 25 grammes. In extreme cases of diabetes much higher amounts have been passed per diem, up to 500 or even 750 grammes. *i.e.* more than a pound.

---

[1] *To make Fehling's solution.*—(1) Dissolve 34·64 grms. pure dry powdered $CuSO_4$ in 200 c.c. distilled water. (2) Dissolve 173 grms. Rochelle Salt (Sodio-potassic Tartrate) in 480 c.c. NaHO., S.G. 1·14. Mix and dilute to 1,000 c.c.

Fermentation test.—The sugar in a diabetic urine undergoes fermentation if left in a warm place mixed with a little yeast; the sugar is decomposed into carbon dioxide and alcohol; $C_6H_{12}O_6 = 2C_2H_6O + 2CO_2$. The amount of sugar present can be roughly gauged from the consequent diminution in specific gravity of the urine; each degree of s. g. lost represents about 1 grain of sugar to the ounce of urine, *e.g.* a loss of 5° s. g. and a daily discharge of 80 ounces of urine gives the day's loss of sugar as 600 grains=about 26 grammes. A more accurate but less expeditious method is to measure the volume or the weight of the CO_2 given off. 1 gramme of CO_2 is equivalent to about 2 grammes of sugar, 100 c.c. of CO_2 are equivalent to about $\frac{1}{5}$ gramme of sugar.

The *polarimeter* is applicable only to very strongly saccharine urine, which should be previously decolorised. Diabetic sugar is dextro-rotatory, and a column of fluid 20 cm. long will rotate the plane of polarisation about 1 degree for each gramme of sugar per cent.

The tests by which blood- and bile-pigments are recognised have been given at pages 32 and 199.

Micturition is a reflex act which can be initiated or resisted by voluntary action. The normal excitant of the act is the distension of the urinary bladder, causing, in consciousness, a desire to micturate. The voluntary response to this sensation may be 'yes' or 'no'—'yes' by contraction of the abdominal muscles, with a passive condition of the sphincter, 'no' by contraction of the sphincter with a passive condition of the abdominal muscles. In the latter case the desire is resisted, and relief is deferred. In the former case the desire is satisfied by a normal act of relief, which commences with contraction of the bladder and of the abdominal muscles, and ends by contraction of the sphincter vesicæ and of the urethral muscles (bulbocavernosus—muscular coat of urethra). In its performance an excitation of the vesical end of the urethra by the first drops of urine, acts as a further stimulus to the reflex act, which may still be inhibited, although with more difficulty.

It may happen—

1. That the excitation is excessive, the desire imperative, the voluntary negative insufficient to arrest the act. Involuntary micturition then occurs, particularly in children.

2. That the sphincter is paralysed. Incontinence of urine is the effect.

3. That the bladder, or that the abdominal muscles, or that both are paralysed; retention of urine in a distended bladder, followed by overflow (= incontinence) are then produced.

4. That the muscles act in an inco-ordinate manner. This condition, which is analogous with 'stammering,' causes temporary retention.

The mechanism of micturition is thus in most respects similar to that of defæcation (*vide* p. 164), the particular points of difference being referable to the fact that whereas the large intestine is of such great capacity that it can retain the fæcal accumulation of many days or even weeks, the bladder is overfilled by the urine secreted in a single day. Consequently the two opposite conditions, retention and incontinence, are usually associated; retention leading to overflow or incontinence, incontinence being the effect of retention. Moreover, micturition is more subject to voluntary control and less influenced by habit than defæcation.

Vesical pressure.—The passive pressure of fluid in a full bladder amounts to about 1 cm. Hg, and it has been found that the sphincter at rest by virtue of its elasticity alone can withstand a vesical pressure of about 3 cm. Hg. A normal man, by the effort of micturition in which the bladder and abdominal muscles are contracted, can raise the pressure to about 10 or 12 cm. A paraplegic patient by the action of the bladder alone can raise it to 4 or 5 cm. The vesical pressures just referred to are not to be confused with the secretory pressure of the kidneys, which, as measured by a manometer connected with a divided ureter of the dog, has been found to reach to about 6 cm.

Excretory action of the liver.—Allusion has been made to the part which the liver plays in excretion; it was mentioned that the bile is not only a secretion serving in digestion, but to some extent an excretion to be got rid of, the most distinct proof of the fact being the identity of urobilin with hydrobilirubin; it was mentioned, moreover, that the liver forms not only bile products (bile-pigments and bile-acids) which are carried away in the bile, but also urinary products (urea, hippuric acid, uric acid) which are carried away in the blood, and separated by the kidneys. We have now to examine this physiological association between liver and kidney as excretory organs; an association which we may at once characterise as formation by the liver, separation by the kidney. The chief items in the argument are the following:—1. Bilirubin is made by the liver. Urobilin is discharged by the kidney. 2. Urea is made by the liver, it is discharged by the kidney. 3. Hippuric acid is made by the liver, it is discharged by the kidney. 4. Uric acid is made by the liver, discharged by the kidney. 5. Sugar, made by the liver, may be discharged by the kidney.

The data upon which these several dicta are based are as follows:—1. Urobilin is chemically identical with reduced bilirubin or hydrobilirubin. 2. A freshly excised liver, submitted to artificial circulation, yields urea found in the outcoming blood. In acute atrophy of the liver with abolition of hepatic function as its consequence, leucin and tyrosin are found in the urine in place of urea. 3. A freshly excised liver, submitted to artificial circulation with a fluid containing benzoic acid, yields hippuric acid found in the outcoming fluid. Benzoic acid taken by the mouth appears as hippuric acid in the urine, but after excision of the liver it passes unchanged as benzoic acid. Hippuric acid is benzoic acid + glycin. 4. After excision of the liver on geese, uric acid ceases to be excreted (Minkowski). 5. Excessive sugar formation by the liver is accompanied by discharge of sugar by the kidney.

The only reservation to be made with regard to the data thus briefly formulated is that urea and hippuric acid are not formed by the liver exclusively; other organs—the kidney in particular—submitted to artificial circulation are also capable of forming these substances, this being especially the case as regards the formation of hippuric acid by the kidney. Still the fact remains that the liver pre-eminently above other organs or tissues, though probably not exclusively of them, is capable of forming urea, and (in birds) uric acid. Matters appear to be on a similar footing as regards bilirubin and urobilin. Although no doubt the principal normal relation is formation of bilirubin by the liver, and separation of urobilin by the kidney, yet we must admit that, failing the liver, urobilin may take origin otherwise in the body.

Excretory action of the skin. Sweat.—The *skin*, by virtue of its glands, is an excretory organ. The substance excreted is almost exclusively water, the amount discharged varying to such an extent with temperature as to cause the urine to be pale and copious in winter, dark and scanty in summer.

The connection between the cutaneous and renal channels of excretion is further illustrated by the appearance of urea in the sweat; even normal sweat is said to contain a trace of urea, and the sweat of a uræmic patient may contain the substance in considerable quantity.

The amount of evaporation taking place from the surface of the body depends upon the physiological activity of the sweat-glands, upon the movements of respiration, and upon the physical state of the atmosphere as regards temperature and pressure, saturation with moisture, and movement of the air. Low temperature, saturation, and stillness are unfavourable, the reverse conditions are favourable to evaporation. Under ordinary conditions air contains about 1 vol. per cent. of water vapour. Air at normal pressure is *saturated*

at 0° by ·65 per cent. water vapour
„ 10° „ 1·8 „ „
„ 20° „ 2·8 „ „
„ 30° „ 4·15 „ „
„ 40° „ 7·25 „ „

e.g. we have seen that the expired air is saturated at 37°, *i.e.* it contains about 7 per cent. water vapour; if into an atmosphere at 1 per cent. saturation a man expires per diem 10,000 litres air, he gives off 600 litres water vapour (=480 grammes).

From the skin the water is given off partly by 'insensible perspiration,' partly as visible drops of sweat, and the latter partly evaporates from the surface, partly trickles off or is absorbed by clothing. The amount of invisible perspiration may be put at 900 litres of water vapour (=720 grammes); that of visible sweat varies greatly.

The secretion of sweat is under the control of sympathetic nerve-fibres which leave the spinal cord by the anterior roots and run a similar course to that of vasomotor nerves. If the peripheral end of the sciatic nerve of a young cat be excited, beads of sweat break out from the pad, and the effect can still be obtained after arrest of the circulation or after amputation of the limb; thus proving the separate existence of sudo-motor nerves

(Luchsinger). As in the case of the salivary gland, pilocarpin stimulates the secretion and atropin stops it. Langley has recently shown that the sympathetic also has action upon the muscles of the hair roots; on the cat stimulation of the lowest sacral and coccygeal roots, or ganglia, causes the hairs of the tail to bristle up to a very unmistakable degree.

Influence of renal action upon tissue-disintegration.—Recent observations by Bradford, although still in progress, and, therefore, not at present susceptible of definite explanation, are, however, of such importance, and so definite as regards the facts themselves, that it is not premature to allude to them here, in further illustration of the evident fact that our precise but rough knowledge of physiological mechanics and chemistry includes only a small portion of the actual phenomena occurring in the living organism, and that we must keep our minds open to the idea that the several parts of the body are interdependent—that their obscure interorganic relations play a most important part in the internal economy of nutrition (p. 220). The facts discovered by Bradford are briefly as follows:—A large wedge of one kidney, amounting to between ½ and ⅔ its total weight, is excised, the surfaces of the remaining portion are fastened together; when the animal (dog) has recovered, the entire second kidney is removed, thus leaving only ⅓ to ½ a single kidney on duty; the consequences of this changed condition are: *acute emaciation* (*e.g.* a fall of body-weight amounting to 37 per cent. in fourteen days), in spite of normal appetite and diet; greatly *increased discharge of water*, and, in less marked degree, *increased discharge of urea.* These effects seem to suggest that the renal function is not merely to remove degradation products, but also to produce some as yet unknown body or bodies, adjuvant of tissue integration, or obstructive of tissue disintegration. We have already recognised that the hepatic gland is concerned in the terminal act of metabolism as well as in its initial phenomena; we are now led to admit that the renal gland plays a part somewhere in the course of metabolism as well as at its final event.

CHAPTER VII

FOOD, NUTRITION, AND EXCRETION. ANIMAL HEAT

PAGE
249 From proteid to urea.
251 From fat and carbohydrate to carbon dioxide. The oxygen deficit.
254 **The Balance of Nutrition.** Import equals export—Gain or loss of Nitrogen signifies gain or loss of flesh—Gain or loss of Carbon signifies gain or loss of fat.
255 Starvation: Export exceeds import. Minimum nitrogen necessary for nitrogenous equilibrium—*Example.* Nitrogenous deficit?—Balance sheet.
258 Influence of age and of 'condition'—Peptone = proteid—Effects of fat—of carbohydrate—of gelatin—alone or added to proteid—Effect of proteid upon fat—of carbohydrate upon fat—of fat upon carbohydrate.
262 **The normal diet of Man:** Effect of food and of work upon excretion of urea.
265 Diet during infancy—Diet during lactation.
267 Alterations of nutrition in disease—*Diabetes*—*Fever*—*Convalescence.*
268 *Hypertrophy* and *Atrophy* of parts and of organs.
269 **Construction and calculation of Dietaries:** A day's food—Food-stuffs—Stimulants—Nourishing value—Cost of N. and of C.

ANIMAL HEAT.

275 *Physical data.* Heat—Temperature—The calorimeter, sources of error—Unit of heat or 'calorie'—Mechanical equivalent of heat—The thermometer—Mass and surface—Specific heat—Latent heat.
278 Animals of constant temperature—of variable temperature—Thermotaxis—Production, distribution, and dissipation of heat—Temperature topography—*Inflammation.*
281 Nerves and nerve-centres concerned in thermotaxis—'Thermogenic?'
283 Normal heat production of man—direct and indirect estimation.
285 The scope of thermometry—*Fever*—Surface and deep temperature—Clinical thermometry. Normal differences with age, sex, time of day, digestion.
288 Heat production '*post mortem.*'

THE living body yields *energy* in the form of *work* and of *heat.* This result is brought about by chemical action. Matter is used up and becomes useless, organic compounds disintegrate and their waste products are got rid of. Consumption of matter is thus a primary condition of vital activity, and it is necessary to the continuance of life that new matter should take the place of spent matter. The food—proteids, fats, and carbohydrates—

supplies the necessary new matter, and is the primary source of all body energy, by its transformation into work, heat, and waste products. The essential waste products are *urea* and *carbon dioxide* ; the essential elements in these waste products as well as in the food are *nitrogen* and *carbon.*

From proteid to urea.—*Nitrogen* enters the body in *proteid* and leaves it in *urea.* In what state or states does it exist in the body, how does nitrogen traverse the body? The answer is necessarily fragmentary and in many respects hypothetical. Proteid by digestion becomes peptone, which is absorbed and retransformed into the proteids of plasma and of lymph. These fluids surround and permeate the organised elements of the tissues, and the proteid which they carry forms the floating balance of nutritive matter from which the comparatively fixed capital of living protoplasm is supplied. Of this *free, circulating, or coasting proteid* in blood and in lymph it is supposed that only a small proportion is actually taken into chemical combination in protoplasm as fixed or *organ proteid,* and that the greater proportion is acted upon and used by living protoplasm without being integrated by it to make part of its own substance. The free or coasting proteid thus used up gives rise to urea, as does that small proportion of fixed or organ proteid which disintegrates and gives place to a correspondingly small proportion of newly integrated proteid. It is supposed that if a superfluous amount of proteid be swallowed, the excess may in the intestine itself by the agency of pancreatic juice be carried beyond the peptone stage and become leucin and tyrosin, which, being absorbed into the portal system, may be at once converted into urea by the agency of the liver. Thus from proteid to urea there are three usual roads: (1) the short cut *viâ* leucin and tyrosin in the intestine, and urea in the liver; (2) the high road *viâ* circulating proteid; (3) the long, narrow way *viâ* circulating and organ proteid. The centre of action is the living tissue element, which, while undergoing little change as to its own proteid, effects considerable change of the proteid solution which soaks through and around it. An analogy may serve to illustrate these alternatives. A sovereign may (1) be changed and spent at once (=excess proteid), or (2) be sent to the bank to form part of a balance which is being used up as required (=circulating proteid), or (3) be invested in comparatively permanent capital (=organ proteid).

Intermediate substances between proteid and urea.—Can we identify any named substances intermediate between proteid and urea? if so, have we any reason to admit that the main current of nitrogen passes in such substances? The second portion of the question may at once be answered in the negative; we find incoming nitrogen in proteid, outgoing nitrogen in urea, but we possess no data enabling us to trace the main current of nitrogen through any named intermediate stage between proteid and urea.

But we may not on this account assert that there are no such intermediate stages, and that urea is immediately derived from proteid; we are to accept the fact that the nitrogenous current is concealed during its passage through the organism, and that we do not know what forms and channels it may take in that passage. It is, however, not totally concealed; we can, among the nitrogenous principles of the body, recognise two or three named bodies in small quantities, less complex than proteid, more complex than urea, and it is allowable to suppose that these bodies are intermediate between proteid and urea, although we are not able to say whether one or all or none are, so to speak, on the main line from proteid to urea. Bodies belonging to this category are *Leucin* and *Tyrosin* (in the intestine), *Glycin* (in glycocholic acid), *Creatin* and *Sarcosin* (in muscle), *Uric acid* and *Hippuric acid* (in the urine).

The relation of leucin and tyrosin with proteid on the one hand and with urea on the other has been already discussed; these bodies are, properly speaking, formed 'outside' the body, although within the digestive tract, and are in no sense to be placed as intermediate stages between proteid in the body and urea emerging from the body. They are named here chiefly because they can appear in the urine in place of urea.

Glycin occurs in glycocholic acid, which is secreted by the liver, re-absorbed from the intestine, and excreted in part as hippuric acid, in part as urea.

Creatin is a natural component of muscle, and is chemically convertible into urea: $\underset{\text{creatin}}{C_4H_9N_3O_2} \underset{+}{+} \underset{\text{water}}{H_2O} \underset{=}{=} \underset{\text{urea}}{CON_2H_4} \underset{+}{+} \underset{\text{sarcosin}}{C_3H_7NO_2}$ but no proof has yet been given that the conversion takes place as a physiological event in the body.

Uric acid is a less fully oxidised product than urea, and may wholly or partially take its place; the nitrogenous excretion of birds and of serpents occurs entirely in the form of uric acid; and in the human subject a characteristic feature of gout is an increased formation of uric acid and a deficient discharge of urea. Neither of these facts proves, however, that uric acid is a normal antecedent of urea.

From fat and carbohydrate to carbon dioxide.—Carbon enters the body in fat and in carbohydrates (starch and sugar) and leaves it in carbon dioxide. It must also be remembered that some carbon enters the body in proteid, and that some hydrogen from fat must leave the body in water. What are the intermediate stages between the initial terms—fat, starch, and sugar—and the final term, carbon dioxide? The answer to this question is necessarily imperfect, for carbon, while in the organism, is hardly less concealed from us than nitrogen. The best attested probabilities are:

1. Carbon in proteid may become carbon with oxygen (CO_2), immediately by the disintegration of proteid, or mediately after the previous formation of fat or of glycogen from proteid.

2. Fat absorbed can exist in the body only as fat, and cannot give rise to proteid or to carbohydrate. The destiny of fat, whether recently absorbed or previously deposited, is to be oxidised, yielding CO_2 and H_2O as its final products. Absorbed fat may thus be immediately expended by oxidation, or it may be stored in the body as a more or less permanent reserve of fat which becomes oxidised when required. Fat so stored as adipose tissue is, although 'fixed,' analogous with circulating albumin in this respect, that it is mainly a neighbour and not a constituent of protoplasm, and there is no positive evidence that fat can contribute to the formation of proteid or be converted into carbohydrate.

3. Carbohydrate absorbed (in the form of maltose) may be immediately oxidised, yielding CO_2, or it may be stored as a comparatively temporary reserve of glycogen in the liver. There is no evidence that carbohydrate forms proteid, and it is doubtful if it ever forms fat in the body, though it certainly favours the deposition of fat (*vide* p. 261). In the muscles it is a possible source of lactic acid, which by further oxidation yields CO_2; it must be admitted, however, that recent observations do not confirm this view, which is in harmony with the accepted doctrine of carbohydrate consumption in muscular activity; on the other hand, the alternative supposition that lactic acid proceeds from

disintegrated proteid is not definitely proved. The above statements, which are no more than a brief summary of the best authorised facts and opinions concerning the general drift of the animal food-supply, may be still further summarised as follows:—

Food	State in body	Chief excretion
Proteid . .	Proteid circulating organised	CON_2H_4
	Glycogen and glucose	CO_2
	Fat	CO_2
Fat . . .	Fat	CO_2
Carbohydrate .	Glycogen and glucose	CO_2
	Fat ? Lactic acid ?	CO_2

Turning our attention to a collateral aspect of the same sequence, viz. to the elementary composition of proteids, fats, and carbohydrates, we shall more fully appreciate two distinct and important points—(1) that a proteid molecule can conceivably be split into a nitrogenous and a non-nitrogenous moiety, as has just been stated; (2) that the 'respiratory quotient' must vary with the nature of the diet, and how so, this being the same problem from its other side, as that which has already been presented to us at p. 131.

(1) The nitrogen contained in 100 grammes of dry proteid amounts to about 15 grammes, and will be contained in 31 grammes of urea; 100 grammes of proteid contain about 50 grammes of carbon, while 31 grammes of urea contain only 6 grammes of carbon; so that in the translation of nitrogen from 100 grammes proteid to 31 grammes urea, a margin of about 44 grammes carbon is left. This carbon may be disposed of by elimination in CO_2, or temporarily stored as glycogen or as fat. We know from experimental data that glycogen and sugar can be formed from proteid, and that fat also can have its source in proteid (pp. 215, 258, 267).

(2) *The oxygen deficit.*—Comparing the composition of a carbohydrate (starch or sugar) with that of fat, we notice that the former contains oxygen and hydrogen in the proportion which gives water, viz. 2H and 1O, whereas on referring to the formulæ of fats we find that the hydrogen is greatly in excess, *e.g.* in palmitic acid we have 32H and 2O. This excess hydrogen in

fat must be oxidised in the body and escape as H_2O. It is accountable for the greater part of the deficit of oxygen in expired CO_2 as compared with inspired O_2. 100 grammes of fat contain about 12 grammes of H and 11 grammes of O. The complete oxidation of 1 gramme H requires 8 grammes O; the complete oxidation of 12 grammes H requires 96 grammes O; so that the oxidation of 100 grammes fat must be supplemented by about 85 grammes O, or nearly 60 litres.

The same holds good of proteids, although in less degree. Referring to the percentage composition of proteids, we find that 100 grammes proteid contain about 7 grammes H and 21 grammes O; 7 grammes H will be oxidised by 56 grammes O, so that the oxidation of 100 grammes proteid must be supplemented by about 35 grammes O, or nearly 25 litres. Thus the total amount of additional oxygen required for the complete oxidation of 100 grammes fat and of 100 grammes proteid will be 85 litres. This amount will go off as H_2O, and be accounted for by a deficit of O_2 in the expired CO_2.

For simplicity's sake we have supposed the oxidation of fat and of proteid in the body to be *complete*; we know, however, that it is incomplete. The supplement of oxygen will therefore be somewhat less than 85 litres; on the other hand a consumption of only 100 grammes each of proteid and of fat is rather below the average, and on referring back to 'Respiration' we find that the difference between inspired O_2 and expired CO_2 has been given as 81 litres. From these considerations it will be evident how the nature of food will affect the amount of oxygen which will be subtracted from external respiration and diverted to the oxidation of excess hydrogen in fat and in proteid, and thus influence the respiratory quotient $\frac{\text{vol. of inspired } O_2}{\text{vol. of expired } CO_2}$. Obviously, the less the subtraction of O by H, the greater the quotient; the greater the subtraction of O, the less the quotient. On a pure carbohydrate diet, the subtraction will be least and the quotient greatest. On a proteid, and *a fortiori* on a proteid *plus* fat diet, the subtraction will be greatest, and the quotient least—relations which are illustrated by the numbers already quoted on p. 131.

It may be asked whether the amount of water given off per diem is greater or smaller than that taken in; to this the answer is that it is *theoretically* greater, although practically the excess is not to be detected—88 litres of O_2 would go off in about 140 grammes H_2O.

The balance of nutrition.—*Import equals export.*—We have learned that the average daily discharge of a man weighing 70 kilos is—carbon 230 grammes, nitrogen 15 grammes, and it is obvious that while a man's weight and health remain constant, this daily export must be made good by an exactly equal import of carbon and of nitrogen in food—*i.e.* an average daily diet must contain at least 230 grammes of carbon and 15 grammes of nitrogen. Such an allowance would be low, and the diet should be estimated on a somewhat more liberal scale, *i.e.* to contain 300 grammes of carbon, and 20 of nitrogen. Still, so long as the weight and state of an animal remain constant, any increase of import must be balanced by an increased export, and under these circumstances 300 grammes of carbon and 20 grammes of nitrogen are necessarily excreted. If an animal gives off less carbon and less nitrogen than it takes in, it must be gaining weight; if it gives off more carbon and more nitrogen than it takes in, it must be losing weight. The first event happens in a young growing animal, the second in a starving animal. Let us consider in further detail the possible modes of departure from the equipoised state of normal nutrition.

Gain or loss of nitrogen signifies gain or loss of flesh.—If during a given period the nitrogen import exceeds the nitrogen export, nitrogen must remain in the body. It does so in the form of proteid, *i.e.* as flesh. An animal under these conditions gains flesh.

If the nitrogen import falls below the nitrogen export, nitrogen must be lost from the body. The animal is losing flesh.

Gain or loss of carbon signifies gain or loss of fat.—If the carbon import exceeds the carbon export, carbon remains in the body. It does so in the form of carbohydrate or fat, probably as fat.

If the carbon import falls below the carbon export, carbon is lost from the body. The animal is losing fat.

In other words a gain or loss of *nitrogen* by the body signifies a gain or loss of *flesh*; a gain or loss of *carbon* signifies a gain or loss of *fat*. And if the percentage composition of flesh and of fat be known, it is easy to calculate how much flesh and how much fat correspond with each gramme of nitrogen and of carbon lost or gained. Flesh contains 3·3 per cent of nitrogen; 1 gramme of nitrogen signifies therefore 30 grammes of flesh. Fat contains 75 per cent. carbon; 1 gramme of carbon signifies, therefore, $1\frac{1}{3}$ gramme of fat.

To what extent do observed facts bear out these theoretical conclusions? The answer to this question is derived chiefly from experiments on the dog: the reason for this choice being that the animal is carnivorous, and can be kept in health during a considerable period upon an exclusively proteid diet (meat); other advantages are, that a dog can be trained to perform definite amounts of work on a treadmill, and to give up the urine either naturally or by catheter when required to do so, and that the error introduced by neglecting losses of nitrogen otherwise than by the kidney, does not amount to more than one to two per cent. of the total nitrogen. On man, the amount of nitrogen eliminated in the fæces amounts to about ten per cent. of the total discharge; on herbivora half the total nitrogen, or even more, may be contained in the fæces.

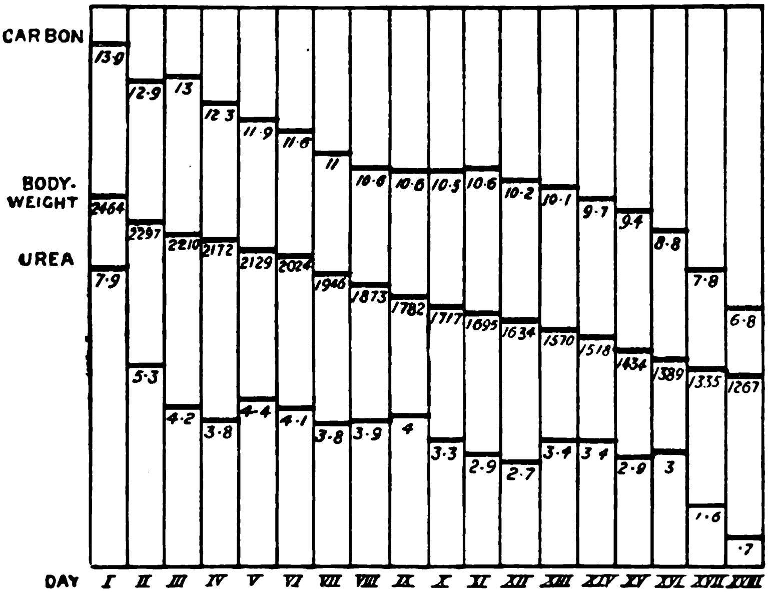


Fig. 100.

Graphic representation of the declining weight and of the daily excretion of a starving cat. (Data by Bidder and Schmidt.)

Starvation.—*Export is greater than import.*—An animal, (*e.g.* a dog or cat) receiving no food, receives no nitrogen and no carbon, yet continues to excrete urea and carbonic acid until the end of its life. In this case there is obviously no equilibrium of nitrogen or of carbon, but an unbalanced expenditure of both. The animal loses flesh, loses fat, and loses weight. The incidence of these losses is well illustrated in the diagrams below. In fig. 100 are given the amounts of carbonic acid and of urea excreted, and the body-weight from day to day of the starvation period. In fig. 101 are given the total loss per cent. of the most important organs and tissues at the end of starvation.

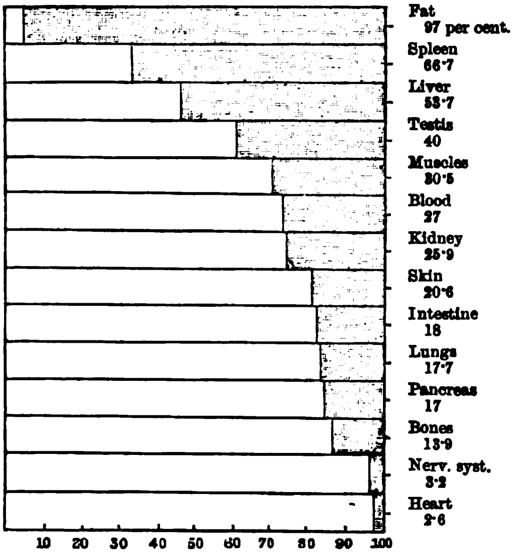


FIG. 101.

Graphic representation of the percentage of different tissues lost during starvation; the shaded areæ represent loss, the unshaded areæ amounts remaining at death. (According to Voit's analyses.)

Minimum nitrogen requisite to nitrogenous equilibrium with an exclusively proteid diet.—It might be expected that, if nitrogen in proteid food equal in quantity to nitrogen excreted during starvation were administered, the loss of nitrogen would be balanced. The expectation would not be confirmed by the event, for the animal would excrete all the more nitrogen, and would require about three times this amount, *i.e.* three times the amount of the starvation export. Then only would import balance export and the animal be in nitrogenous equilibrium. Beyond this minimum amount, a further increase of food-nitrogen would still be balanced by a corresponding increase of excreted nitrogen, and the animal would continue to be in nitrogenous equilibrium. Excessive amounts of meat would be liable to cause diarrhœa and thus put an end to the observation. But from 'minimum' to 'excessive' the range is considerable; nitrogen equilibrium is maintained with nitrogen imports of considerable magnitude; this is the normal state of a healthy or even of a voracious man, his nitrogen import is far above the minimum necessary, but is balanced by a correspondingly large nitrogen export, and he remains in nitrogenous equilibrium, although a breakdown of his kidneys or an attack of gout may be close at hand. Exact experimental results relating to nitrogenous equilibrium are, however, possible only on carnivorous animals—usually dogs.

Example.—A dog weighing 10 kilogrammes excretes during the first days of starvation about 5 grammes of nitrogen per diem. This amount of nitrogen would be contained by about 150 grammes of meat. In accordance with what has been said above, a daily allowance of 150 grammes meat, containing only just as much nitrogen as is contained in the starvation export, would be insufficient to balance the daily loss. The excretion of nitrogen would be increased, and would be in excess of the nitrogen income of 5 grammes derived from 150 grammes of meat. It would be between 5 and 10 grammes, and the animal on the daily allowance of 150 grammes of meat would continue to lose flesh and eventually starve. Nitrogenous equilibrium would not be reached until nearly 500 grammes of meat are given per diem, and now the import and export of nitrogen would each be about 15 grammes. As already stated above, nitrogenous equilibrium is not obtained until the food contains about three times the amount of nitrogen excreted when no food is given, and in the case of a carnivorous animal fed upon meat, the daily ration must amount to about $\frac{1}{20}$ the body-weight of the animal. Beyond this minimum (500 grammes meat) the animal is capable of disposing of an additional quantity, still remaining in nitrogenous equilibrium; 1,000 grammes may be the daily ration consumed; in this case the nitrogen of the food and the nitrogen of the excreted urea will each amount to about 30 grammes per diem.

Nitrogenous deficit.—In the above example the nitrogen income and outgo balance each other; there is no deficit on either side. But in many experiments the two quantities have been found not to balance; the amount of nitrogen exported in urea has been found to fall short of the nitrogen imported in proteid.

The deficit has been accounted for as being due to the discharge of nitrogen in a gaseous state by respiration. The fact has, however, not been proved—the amount of NH_3 in expired air is infinitesimal, about ·001 grm. per hour—and we have against it the observations of nitrogenous equilibrium with varying quantities of proteid food. It appears most probable that the so-called nitrogenous deficit is only apparent, and due to errors of analysis.

Returning to our example, let us consider the carbon equation and the body-weight of the dog weighing 10 kilogrammes. During total deprivation of food the dog is obviously losing flesh, losing fat, and losing weight. With the insufficient allowance of 150 grammes of meat, the dog is still suffering the same losses, but less rapidly. With the sufficient diet of 500 grammes, the dog is neither losing nor gaining flesh, but may be losing or gaining weight. 500 grammes of meat contain nearly 70 grammes of carbon, and it is possible that the respiration of the animal is such that more or less than this amount is exported as carbon dioxide—if more, the animal is losing fat and losing weight; if less, the reverse is the case. With the more than sufficient allowance of 1,000 grammes, and the animal in nitrogenous equilibrium, it is probable that the carbon export will not amount to the carbon import, and the animal will consequently be putting on fat and gaining weight. The value of this increase, and in the case of the 500 grammes allowance, whether there is increase or decrease, is to be ascertained by measuring the amount of CO_2 excreted per diem.

These statements will be made clear by considering the accompanying balance sheet, which gives the nitrogen and carbon with inadequate, adequate, and more than adequate diets of meat given to a small dog. The excretion of nitrogen otherwise than in urea, is omitted from consideration as being a negligible quantity.

Influence of age.—The case of the dog on a diet of 500 grammes of meat is deserving of some further consideration. The amount is that theoretically the smallest adequate to the maintenance of a 10-kilogramme dog in nitrogenous equilibrium. It would be found that, other things being equal, a

Dog weighing 10 Kilogrammes

Daily income	N	C	Daily expenditure	N	C	Remarks
I. None	0	0	Urea 10·7 grammes .	5	2	The dog is starving rapidly, losing per diem 5 grammes N. and 32 grammes C., equivalent to 150 grammes flesh and 23 grammes fat.
			CO_2 110 grammes .	0	30	
			Total . . .	5	32	
II. Meat 150 grammes	5	20	Urea 15 grammes .	7	3	The dog is still starving, losing per diem 2 grammes N. and 22 grammes C., equivalent to 60 grammes flesh and 30 grammes fat.
			CO_2 143 grammes .	0	39	
			Total . . .	7	42	
III. Meat 500 grammes	16·6	66·6	Urea 35·6 grammes .	16·6	7	The dog is in nitrogenous equilibrium, neither gaining nor losing flesh. The dog is also with the above carbon values neither gaining nor losing fat. It would, however, be found in an actual experiment that, whereas the nitrogen export would remain practically constant and in equilibrium with import during many days, the carbon export would vary considerably, implying if above 67 grammes a loss of fat, if below 67 grammes, a gain of fat.
			CO_2 220 grammes .	0	60	
			Total . . .	16·6	67	
IV. Meat 1,000 grammes	33	133	Urea 70 grammes .	33	14	The dog is still in nitrogenous equilibrium, neither gaining nor losing flesh, but gaining fat at the rate of 58 grammes per day (14 grammes C.). The animal is gaining weight with this deposition of fat. The experiment is likely to terminate with an attack of diarrhœa, an event which would be retarded by allowing the dog plenty of exercise.
			CO_2 275 grammes .	0	75	
			Total . . .	33	89	

young dog would require a higher minimum than an old dog, and we recognise in this fact an experimental illustration of what experience shows to be requisite in the feeding of children, who require a larger proportion of proteid than do adults, taking into account the difference of body-weight. Thus the mixed diet of an adult should contain 2 grammes of dry proteid per kilogramme body-weight, while that of an infant 1 year old should contain double that amount, viz. 4 grammes per kilogramme body-weight. The *state of nutrition* is also an influential factor; other things being equal, an ill-nourished animal is accommodated to and requires per diem a smaller allowance than a well-nourished animal, and the same animal passing from a well to an ill-nourished state gradually accommodates itself to a lower minimum, while in passing from an ill to a well-nourished state it requires an increasing minimum allowance, and becomes able to tolerate and dispose of a larger excess above that minimum. We recognise in these facts experimental illustration under simple conditions of what takes place in man under more complex conditions; many poor persons are accommodated to a much lower minimum than that which would be necessary to keep a well-to-do person in good condition; many well-fed persons are accommodated to a much higher minimum, and can tolerate an excess diet far greater than could be suddenly disposed of by an ill-fed individual. Such persons, however, run the risk of becoming overloaded with uric acid, or of overworking their kidneys; they are liable to be purged of undigested food by diarrhœa, or they find it necessary to habitually stimulate a 'sluggish' digestion, and exercise, instead of being the effect of natural inclination, becomes to them a hygienic observance.

Peptone=Proteid.—The experiment has been made of substituting peptones for undigested proteid in the feeding of dogs. It has been found that peptones are capable of taking the place of proteid, and that dogs fed with peptones alone can grow and fatten and be kept in nitrogenous equilibrium.

Effects of fat, carbohydrate or gelatin, added to proteid.—If in addition to proteid an experimental diet is made to include fat or starch or gelatin, it will be found possible to establish nitrogenous equilibrium with a smaller quantity of proteid than when the latter is administered alone. In the case of the 10-kilogramme dog requiring per diem at least 500 grammes of meat to be brought into nitrogenous equilibrium, the result would be obtained with half that quantity of meat *plus* 50 grammes of fat. Each of the above-named substances, fat, carbohydrate, and gelatin, are the natural allies and companions of proteids in normal diets; although administered alone, none of these substances can support or even prolong life; an animal fed with fat, or with carbohydrate, or with gelatin, or with all these substances *sine* proteid, will speedily die of starvation.

Effect of proteid upon fat.—Fat alone cannot support life; added to proteid, it economises the latter as above stated. As regards the converse relation, proteid administered with fat accelerates the consumption of fat; similarly proteid administered in considerable quantity to a fat animal, accelerates the consumption of fat, and the animal loses fat. The Banting system of treating obesity by a diet containing abundant proteid and restricted fat and carbohydrate, is based upon this principle. But it should be remembered that under certain conditions, viz. administered in large quantity to a purely carnivorous animal, proteid alone can fatten. We saw an instance of this in the case of the well-fed dog; on man, however, it is not possible to verify the fact, as a pure proteid diet cannot be maintained. We must nevertheless remember that fat in the body may have proteid in the food as an antecedent, although the chief relation between the two is that proteid accelerates expenditure of fat, while fat economises or obstructs the expenditure of proteid.

Effect of carbohydrate upon fat.—The popular notion that 'sugar is fattening' appears to be borne out by experiment. There can be no doubt that carbohydrates do promote the fattening of cattle; the analyses of Lawes and Gilbert have placed this point beyond a doubt. These observers estimated the amount of fat put on by cattle during a given time, in comparison with the amount of fat contained in the food consumed during the same time, and found that the amount of fat gained was more than four times as great as the amount of fat contained in the food. Whence could the fat be derived? It might have been from proteid, or it might have been from carbohydrate, and it cannot be positively stated from which of the two sources it proceeded. This much is certain, that carbohydrate was essential to the fattening, but it is an open question whether it produced this result (1) by direct conversion of carbohydrate into fat, or (2) by economising the combustion of body-fat laid down from accompanying proteid. The first alternative is generally regarded as the more probable, although as yet it is not an undisputed conclusion. It is to be remembered that, although carbohydrates fatten, they cannot entirely replace fat in the diet of man.

Effect of fat upon carbohydrates.—Fat in the food, if it enters the body, is oxidised at once, or holds its place as fat. There are no observations to show that it can become or give rise to either proteid or carbohydrate in the body. All observers are agreed that fat does not assist in forming glycogen in the liver; Seegen indeed states that fat may directly form sugar in the liver, but his observations are unconfirmed.

The normal diet of man.—It is best, and, indeed, absolutely necessary, that human food should include *proteids*, *fats*, and *carbohydrates*, to which must be added *salts*, *oxygen*, and *water*. The absence of any one of these proximate principles kills by starvation. Absence of oxygen kills in two or three minutes, absence of water in a few days, absence of proteid or fat or carbohydrates in two to three weeks, and the absence of salts cannot be endured for a much longer period. That common salt is one of the necessaries of life is attested by the risks which men have run to obtain it when scarce, and by the 'salt-licks' frequented by wandering troops of animals.

How little can a healthy man endure life upon, and how much must be given to him if he is to be kept efficient? The answer is afforded by the dietaries of armies, prisons, and gangs of navvies. In round numbers, and omitting circumstantial considerations, the minimum daily income of a man in full work must be about 5 per cent. of his body-weight, viz.,

Solid food	1 per cent.
Oxygen	1 „
Water	3 „

That is to say, a man of 70 kilogrammes must get

Solid food = 700 grammes
Oxygen = 700 „
Water = 2100 „
Total = 3500 „

The 700 grammes of solid food should contain about

140 grm. proteid
105 grm. fat
420 grm. carbohydrate
35 grm. salt.

Or, to reduce those numbers to an easily remembered form, from which the adequate diet of men of different weights can be estimated, it should contain per one kilogramme body-weight, 2 grm. proteid; 1·5 grm. fat; 6 grm. carbohydrate; 0·5 grm. salt, in all 10 grammes, or *one per cent.* of solid food.

These numbers are applicable to normal adults doing ordinary work. The estimate is a liberal one, especially as regards the proteid. Voit gives as adequate:—Proteid 118 to 137; fat 56 to 117; carbohydrate 352 to 500. Ranke's 'normal diet' is:—Proteid 100; fat 100; carbohydrate 240 grms.

The chief conditions which will modify the amounts of an adequate diet are *work*, *health*, and *age*.

Effect of work.—A person doing no work at all will subsist upon amounts somewhat smaller than those given above; a person engaged in exceptionally heavy work (soldier in the field, prizefighter, navvy, &c.) will require larger amounts.

No work	6·6 gr.	solid food	per 1 kg.
Ordinary work 100·000 kgm.	10	„	„
Hard work 150·000 kgm. . .	15	„	„

With regard to the most important constituent, viz. the proteid, authorities differ, and their statements are apt to be misunderstood. Playfair's tables lay down as proteid allowances numbers in direct proportion with work done, and it is obvious that these numbers were inspired by the now discarded theory that muscular work depends upon, and is in direct ratio with, disintegration of proteid; but as will presently be seen, muscular exertion causes no appreciable increase in the excretion of urea. The discrepancy may be reconciled by the following considerations: A strong labouring man requires a larger amount of proteid to supply his muscular mass than a sedentary man; the man who is fit to be a soldier or a navvy must be allowed more proteid than the man who is at the physical level of a tailor or a clerk; a convict who is fit for hard labour must be put upon a higher proteid diet than one who is unfit. But there is no appreciable difference in the proteid requirements of a muscular man whether he works or rests; he should get, say, 140 grammes proteid in either case; nor in those of the non-muscular man, whose tissue requirements will be fulfilled by, say, 80 grammes, whether he works or rests. The differences in the amounts of proteid allowed in 'light labour' and 'hard labour' prison diets, in army diets, and in workhouse diets, are thus theoretically justified, and for all practical purposes near enough to the actual necessities of the different classes of men.

As regards the carbonaceous constituents (fat, starch, sugar) the facts are different; amount of work and amount of carbon used are in direct relation. Whereas the nitrogen requirements of a given individual persist practically constant in work and out of work, the carbon requirement and the carbon consumption rise and fall with work and rest. The same man gives out more CO_2 during work than during rest, and if a labourer keeps at work for a week, he must have a larger daily allowance of carbon in his food than would be sufficient during a week of complete laziness. A clerk probably gives out more CO_2 and consumes more carbon per diem during his holiday than he does during a day of his ordinary employment. This is in complete contrast with the nitrogen requirement, and has already been sufficiently explained under 'Respiration' (p. 130).

Effect of food upon excretion of urea.—The amount of nitrogen excreted in urea is directly dependent upon the amount of nitrogen taken in proteid. A dog, taking 500 or 1,000 grammes of meat, eliminates 35 or 70 grammes of urea, and if one day he takes and digests double the amount of proteid he will during the next day excrete about double the amount of urea. The condition of the dog or man is one of nitrogenous equilibrium, or in other words the amount of urea excreted is in direct relation with the amount of eaten and digested proteid.

Effect of muscular exercise upon excretion of urea.—It might be expected that great muscular exertion should be attended with a disintegration of muscle and a corresponding increase in the amount of urea excreted. The expectation has not been verified by experiment. Muscular exertion *per se* gives rise to no marked increase of urea excreted, in other words there is no demonstrable relation between amount of work done and amount of urea excreted. The best known observations in justification of this statement are those of Fick and Wislicenus upon themselves, and those of Flint and of Pavy upon a pedestrian. But while we must admit that the discarded doctrine of a ratio between work and wear of muscle, as evidenced by urea, is incorrect, we must also admit that the contradictory doctrine has been expressed too absolutely. Recent experiments show that urea excretion does vary a little with muscular action, although the variations are so small as to be easily swamped and hidden by the larger fluctuations due to variations of diet (Argutinsky, Pflüger); and Zuntz's observations are to the effect that muscular exercise, if excessive—*i.e.* if pushed to the point of producing dyspnœa—

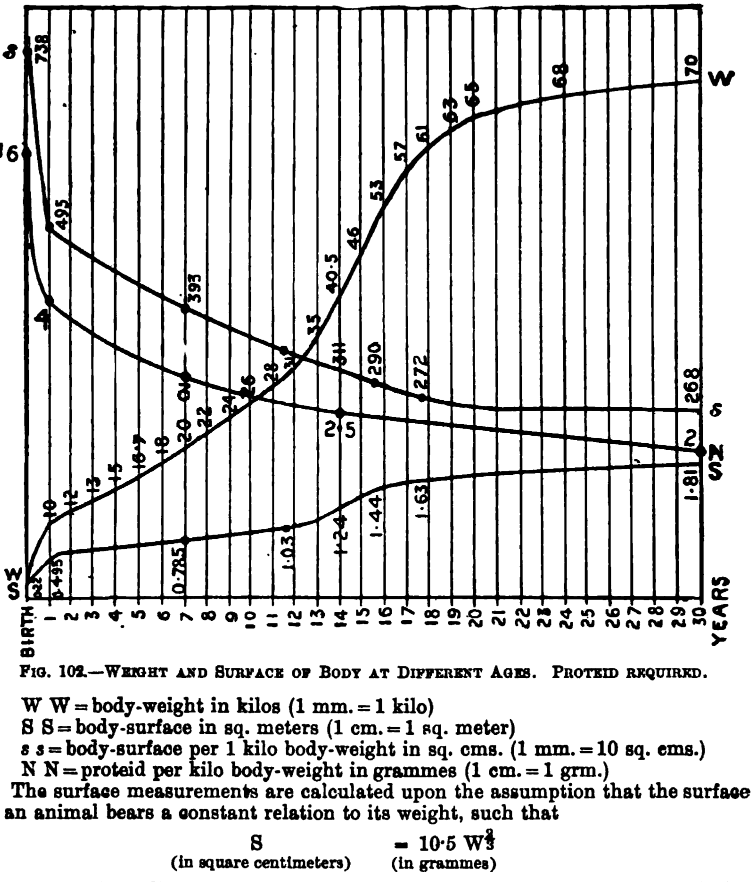


FIG. 102.—WEIGHT AND SURFACE OF BODY AT DIFFERENT AGES. PROTEID REQUIRED.

W W = body-weight in kilos (1 mm. = 1 kilo)
S S = body-surface in sq. meters (1 cm. = 1 sq. meter)
s s = body-surface per 1 kilo body-weight in sq. cms. (1 mm. = 10 sq. cms.)
N N = proteid per kilo body-weight in grammes (1 cm. = 1 grm.)

The surface measurements are calculated upon the assumption that the surface of an animal bears a constant relation to its weight, such that

$$\underset{\text{(in square centimeters)}}{S} = \underset{\text{(in grammes)}}{10{\cdot}5\,W^{\frac{2}{3}}}$$

The average heat-discharge per square centimeter per diem is nearly 150 calories (or $\frac{1}{10}$ cal. per minute); so that the surface of an animal body in square centimeters, multiplied by 150, gives the value in calories of the daily heat-discharge.

causes disintegration of organ-proteid, and increased discharge of urea.

Diet during infancy.—A child or infant requires absolutely less food than a full-grown man, but relatively to their respective body-weights a much larger quantity. Thus it would not be sufficient to give to a child of 7 or 14 kilos only $\frac{1}{10}$ or $\frac{1}{5}$ the amount required by a man of 70 kilos, and we should find in drawing up a diet-table for children at different ages, that the area of the body-surface is a far better proportional indicator than the body-weight. This is especially the case as regards proteid, and will be evident on examination of the table below.

Age	Body-weight	Body-surface	Total dry proteid per diem	Do. per kilogramme body-weight	Do. per sq. meter body-surface
	kilogrammes	square meter	grammes	grammes	grammes
Birth	3	0·22	18	6	90
1 year	10	0·5	40	4	88
7 years	20	0·8	62	3	87
14 ,,	40	1·24	100	2·5	88
30 ,,	70	1·8	140	2	85

The last two columns of this table show that in proportion to body-weight the amount of proteid required by an infant is greater than that required by an adult, while in proportion to body-surface it is approximately constant (viz. between 80 and 90 grammes per square meter). As regards other constituents the best guide to their amounts is the composition of milk, which is normally the only food required by infants during the first months of life. In round numbers human milk contains, per 100 c.c.

3 grammes proteid
3·5 ,, fat
5 ,, sugar

An infant at the breast must therefore take per diem 500 to 1,000 c.c. of milk to get

15 to 30 grammes proteid
20 to 40 ,, fat
25 to 50 ,, carbohydrate

If artificial feeding is required, cow's milk is usually first resorted to, and seeing that cow's milk is, as compared with human milk, richer in fat and proteid, poorer in sugar, it is necessary to dilute it and to add sugar to it. A common error in the feeding of infants is the premature augmentation of the carbohydrate element, 60 to 90 grammes carbohydrate being the amount commonly given in diet-tables to correspond with 20 to 36 grammes proteid. The composition of milk, is, however, such as to indicate that the carbohydrate should not largely exceed the proteid constituent, during at any rate the first 9 months of life. After this period the requirements may be regarded as approximating towards those of the adult, in whom, as we have seen, the amount of carbohydrate required is three times that of proteid.

A growing infant excretes less carbon and less nitrogen than it takes in; it gains in weight and puts on both flesh and fat; during the first year of its life it gains about 7 kilos. Taking half of this amount to be flesh, this would mean a gain of about 120 grammes nitrogen, *i.e.* $\frac{1}{3}$ gramme per diem; the average proteid income of 30 grammes contains about $4\frac{1}{2}$ grammes nitrogen; the amount of nitrogen kept back in the flesh of a growing infant up to the end of the first year of life is thus about $\frac{1}{13}$ of the nitrogen contained in the total proteid consumed; during the second year it is about $\frac{1}{60}$, during the third about $\frac{1}{140}$.

Diet during lactation.—Consider the case of the mother, supposing her to weigh 50 kilos, and to receive an average proteid allowance of 100 grammes. If she is to supply a child with one litre of milk containing 30 grammes of proteid per diem, she should receive an addition of about 90 grammes to her food, *i.e.* her day's proteid should amount to nearly 200 grammes, a requirement which is recognised in the official instructions issued in France to persons employing a wet-nurse, to the effect that she must receive nearly twice as much food as an ordinary woman. While nursing she will also excrete considerably more urea than in her normal state.

That so large an increase in the proteid allowance should be requisite during lactation is no less apparent if we consider the facts already alluded to concerning the relation between proteid and fat. We have seen that proteid can fatten, that 100 grammes proteid contain about 44 grammes of surplus carbon, which may go to form fat or carbohydrate; now it is shown both by experience and by experiment that not fat but proteid is the substance from which milk-fat is formed. The day's milk yielded by a wet-nurse contains, say, 30 grammes of proteid and 40 grammes of fat; the proteid supplement to her ordinary diet is, say, 90 grammes; of this amount 30 grammes are accounted for in the milk; the remaining 60 grammes contain 9 grammes nitrogen (which will go off in about 20 grammes urea), and 27 grammes surplus carbon (which might form part of 36 grammes fat). This is as good an illustration as can be desired, showing that the proteid molecule can split into a nitrogenous moiety, urea, and a non-nitrogenous moiety, fat. In the case just considered 90 grammes of food proteid have reappeared as 30 grammes of milk proteid + 37 grammes of fat + 20 grammes of urea.

Alterations of nutrition in disease; diabetes; fever; the con-

valescent state.—The food requirements of the body are, as a rule, much diminished in disease; the activity of the tissues is depressed, little or no external work can be done, and diet must be calculated on a much lower scale.

There are, however, certain exceptions to the general rule: in *diabetes*, the amount of food and of water which are 'consumed' is sometimes enormous, but is it really consumed in a physiological sense, that is to say, utilised in the nutrition of tissue? The wasting and loss of body-weight, the excessive discharge of sugar and of water, and, in certain cases, the degeneration of proteid into fat, and, finally, the incapacity of diabetic subjects to perform work, all go to show that the body is then incontinent of food, which its tissues fail to assimilate.

In *fever*, as a rule, we find that much less solid food is consumed, while the demand for water is increased. Here, again, the tissue waste is increased, morbid products are formed, and the increased demand for water may be viewed as the attempt of the organism to wash itself clean; copious perspiration is a sign of success, and a token that the critical point has been turned. In *convalescence* from fever, we have a true instance of increased nutrition; the tissues have wasted during invasion, and when released from the oppressive agencies reassert their want of food to an enhanced degree; 'appetite' is good, more food is consumed by the mouth, and consumed in the tissues, the body-weight rises again and strength returns; the chief danger is that the renewed appetite of the tissues should overtax the digestive organs which have shared in the general depression.

Hypertrophy and atrophy of parts and of organs.—If a limb or organ is more than usually exercised, it grows larger than usual; if it is less than usually exercised, it dwindles and becomes smaller than usual. The first event is called hypertrophy, *i.e.* overnutrition; the second, atrophy, *i.e.* deficient nutrition; and these effects, which we can see, and touch, and trace back to evident causes, give us an insight into the normal process which we could not otherwise obtain. A part which is more used gets more 'food;' its vessels dilate, and the blood-flow is increased in response to the necessities of the tissues. A part which is less used gets less food; its vessels contract, and the blood-flow is diminished. In either case, the supply is adjusted to the demand through the agency of afferent and efferent nerves.

Experimental and pathological illustrations of both processes are abundant. If the cervical sympathetic of a young rabbit be divided, the vessels of the ear on that side dilate, more blood passes through the part, and the ear grows faster and larger than on the other side. The skin round an old-standing sore may become thicker and more hairy in consequence of the increased blood-supply in the neighbourhood of the irritation. The spur of a cock transplanted from the leg to the comb grows to an extraordinary degree, because it gets more blood than usual.

Instances might be multiplied. Any hollow viscus grows larger and thicker if the channel from it is narrowed; any limb or single muscle grows bigger if its daily work is increased, on the principle—more work, more food, more tissue. Hypertrophy of the heart, of the bladder, of the intestines, the disproportionately well-developed legs of a ballet-dancer, or arms of a blacksmith, the contrast between the muscles of a navvy and those of a clerk, all illustrate this principle. The converse effects are no less marked, though, perhaps, less striking and apparent; the consequences of atrophy or deficient nutrition are to be seen in every old person, in less active organs, less work, less active circulation, in dwindling and degenerating tissues.

That food-supply by blood to tissue is controlled and measured out by nerves, we have already learned from the study of vasomotor action; whether the intimate processes of tissue nutrition are governed by nerves, we shall inquire when we come to study the obscure question of *trophic nerves.*

Construction and calculation of dietaries.—The proximate principles—proteids, fats, and carbohydrates—convey into the body the necessary nitrogen and carbon, and are themselves conveyed into the body in the various food-stuffs or articles of diet in common use. Without entering into any minute description of the properties and qualities of all the articles of food which may be named on a bill of fare, we will very briefly consider one or two staple food-stuffs, and point out how diet-tables should be made use of in order to calculate an adequate food allowance, *i.e.* an allowance not far short of **20 grammes nitrogen** and **300 grammes carbon.**

Food-stuffs.—It should be said in the first place that the proteid or nitrogenous principles can be derived from animal and from vegetable sources; that, of the non-nitrogenous principles, fats are also derived from both sources, while carbohydrates are of entirely vegetable origin, with the exception of milk-sugar, and omitting glycogen, as not being contained in *ordinary* food-stuffs.

APPROXIMATE COMPOSITION OF SOME COMMON ARTICLES OF DIET
(Compiled chiefly from Parke's tables).

Food-stuffs	Proximate principles				Elements	
	Water per 100	Proteid per 100	Fat per 100	Carbo-hydrate per 100	Carbon per 100	Nitrogen per 100
Milk	86	4	4	4	7	0·6
Butter	7	1	92	—	70	0·15
Eggs	75	14	10	—	15	2
Beefsteak	70	22	5	—	15	3·3
Bread	40	8	1·5	50	27	1·25
Potatoes	75	2	—	21	10	0·3
Oatmeal	15	12	5	65	40	2
Dried peas	15	22	2	60	40	3·3
Rice	10	5	1	83	40	0·75
Cocoa powder	10	15	50	25	55	2·2
Cheese	40	35	25	—	35	5·2
Beer	90	1	—	10	5	0·15

Referring to the table, the following points are to be remarked. The chief nitrogenous food-stuff is meat, but many vegetables, *e.g.* peas, are not inferior to meat as regards the percentage of nitrogen they contain. This does not imply, however, that the nutritive value of peas is equal to that of meat; most people will absorb 3·3 grammes of nitrogen more easily from 100 grammes of meat than from 100 grammes of split peas. All the nitrogenous food-stuffs contain carbon as well as nitrogen; this we already know from the composition of proteids, which contain about 50 parts of carbon to each 15 parts of nitrogen. Of the 'non-nitrogenous' food-stuffs, only butter, which is the fat of milk, and the ordinary fat which is attached to meat, are literally non-nitrogenous. Vegetables, such as potatoes, are the chief source of the non-nitrogenous carbohydrate, but they are not non-nitrogenous food-stuffs, inasmuch as they also contain nitrogen. Bread in particular, the most important of all food-stuffs, contains nitrogen as well as carbon.

The desirable proportion between nitrogen and carbon in a diet is accepted to be $\frac{1.N}{15.C}$ by weight. In meat the proportion is about $\frac{1.N}{5.C}$; so that if a person should attempt to live upon meat only, he must swallow too much nitrogen if he is to get a right amount of carbon, or too little carbon if he is to get a right amount of nitrogen. In bread the proportion is about $\frac{1.N}{22.C}$; so that if a person should be restricted to bread only, he must swallow too much carbon if he is to get a right amount of nitrogen. But while neither of these food-stuffs alone yields the right proportion, both together will do so, and in ordinary life meat and bread are taken together, these two food-stuffs constituting the foundation of every prosperity diet, to which they contribute nearly all the nitrogen and three-fourths of the carbon. Theoretically, indeed, it would be possible to obtain exactly the right amounts of carbon and of nitrogen by duly adjusted amounts of these two staple articles, meat and bread, but practically it is necessary to take into account a due proportion of fat, which has by experience been proved indispensable to the maintenance of health, and not fully replaced by carbohydrate. Considerations of cost and of taste will also have to be taken into account.

A day's diet.—As the foundation of a day's diet we may put down

	Carbon	Nitrogen
Bread, 1 pound (450 grammes) . . .	117 grms.	5·5 grms.
Meat ½ pound (225 grammes) . . .	34 ,,	7·5 ,,
Making a total of . .	151 ,,	13 ,,

The chief deficiency here is of the carbon; nitrogen is also defective, but less so, though not less so than in many a necessity diet; we are, however, at this moment constructing the diet of a properly fed healthy active man.

Theoretically as well as practically the foundation from which we have started will be completed by fat (with the meat, or as bacon or as butter); from all sources about ¼ lb. (112 grammes) containing 84 grammes carbon.

The diet is now

	Carbon	Nitrogen
Bread, 1 pound	117 grms.	5·5 grms.
Meat, ½ pound	34 ,,	7·5 ,,
Fat (butter, bacon, &c.), ¼ pound .	84 ,,	— ,,
Making a total of .	235 ,,	13 ,,

This foundation is ordinarily supplemented or in part replaced by a variety of articles, the most important of which are *potatoes, rice, eggs, milk, cheese, oatmeal, peas, beans, and cocoa.*

Potatoes to a certain extent replace bread and butter; they are especially a carbon supply, also—but in a very low proportion—

a nitrogen supply. One pound of potatoes (450 grammes) contains 45 grammes carbon and 1·3 nitrogen. An Irish labourer consuming 10 pounds of potatoes per diem, and nothing else, would get 450 grammes carbon and 13 grammes nitrogen, but he would be 'ill-fed.'

Cheese is a very prevalent substitute for meat among agricultural labourers; ⅛ lb. of cheese (56 grammes) contains 20 grammes carbon and 3 grammes nitrogen. *Half-a-pint of milk* (283 c.c.) contains about 20 grammes carbon and nearly 2 grammes nitrogen. *Two eggs* (weighing about 100 grammes) contain about 15 grammes carbon and 2 grammes nitrogen.

Peas, beans, and lentils are to be mentioned as forming the backbone of a vegetarian diet, in which they take the place which meat occupies in ordinary diet, forming the chief nitrogen supply. *Rice* is mentioned because it is a staple article of food among Eastern nations; *oatmeal* because of the important place it holds in the dietary of North Britain. But, seeing that all these articles are accidental rather than habitual items in ordinary English life, we shall not take them into account in this connection.

Adding some of the preceding accessories to our fundamental diet we have as an ideal complete diet:—

		Carbon	Nitrogen
Foundation	1 pound bread . .	117 grms.	5·5 grms.
	½ pound meat . .	34 ,,	7·5 ,,
	¼ pound fat . . .	84 ,,	—
Accessories	1 pound potatoes . .	45 ,,	1·3 ,,
	½ pint milk . . .	20 ,,	1·7 ,,
	¼ pound eggs . . .	15 ,,	2 ,,
	⅛ pound cheese . .	20 ,,	3 ,,
		335 ,,	21 ,,

This is a liberal diet with a margin above the normal, but it is somewhat costly, viz. at ordinary market prices nearly one shilling.

More detailed consideration of diet belongs to practical medicine; all that is desirable from a physiological standpoint is to realise certain fundamental principles and certain prominent illustrations of these. It is important to become familiar with the use of tables of food analysis with clear knowledge of the essential points which should be looked for. The short table used above in the construction of a normal diet, gives in round numbers the compositions of the commonest food-stuffs rated in proximate principles and in their two important elements of income. We may use this table again to estimate the nitrogen and carbon values of a hospital 'ordinary' diet, *e.g.*:—

	Carbon	Nitrogen
2 pints of tea (with sugar) (1,134 c.c.)	? 25 grms.	— grms.
½ pint of milk (283 c.c.)	20 ,,	1·7 ,,
1 pint of beef tea (567 c.c.)	? 7 ,,	? ·6 ,,
4 oz. cooked meat (113 gms.)	20 ,,	4 ,,
½ lb. potatoes or vegetables (225 grms.)	22 ,,	·7 ,,
¾ lb. bread (339 grms.)	75 ,,	4 ,,
¾ oz. butter (21 grms.)	16 ,,	— ,,
Sum total	175 ,,	11 ,,

Obviously this sum total must be inadequate to sustain life in a large percentage of cases, especially if not confined to bed and entering upon convalescence, and as a matter of course it is supplemented by the liberal allowance of 'extras.' We may add for the sake of comparison the following figures:

	Carbon	Nitrogen
'Starvation diet' (East-end needle-woman)	200 grms.	9 grms.
'Almost starvation diet'	264 to 270 ,,	11 to 13 ,,
'Light labour' prison diet	295 ,,	14 ,,
'Hard labour' prison diet	335 ,,	16 ,,
Fairly nourished operatives	390 ,,	22 ,,
Military prison diet	340 to 400 ,,	18 to 20 ,,

All these diets are too low to sustain life at a normal level of energy for any prolonged period in the various classes of persons to whom they are administered. Flagging energy and loss of flesh are quickly produced in the first three examples, and even in the last three it has been found necessary to raise the diet or to lower the labour.[1]

The factors of nourishing value.—To properly estimate the nourishing value of a food we must take into account not merely its percentage of carbon and nitrogen, but also its palatability and its digestibility. A 'nourishing' food must not only be chemically adequate, it must also be palatable and digestible. It may possess any one, or even two, of these three essentials and yet not be nourishing. Thus dried peas and beans or even horse chestnuts and acorns are chemically adequate, but they are not palatable. Cheese and hard-boiled egg stand high as regards chemical value, but are very indigestible. Conversely it may happen that a substance is particularly digestible, so that it has a nourishing value which its chemical composition would not have led us to expect; gelatin, for instance, in the form of calves'-foot jelly, is of indisputable practical value in the nourishment of the sick.

---

[1] The veil which measurements in pounds, ounces, pints, and grains, casts over a diet-table, is best removed by converting them at once into grammes and cubic centimeters, and then proceeding to take percentages. Of course this calculation may be made directly from the old measures, but the results do not come out so quickly and clearly. It is easier to estimate diets by elements than by proximate principles, heed being taken that carbon has a higher value in fat than in carbohydrate.

Stimulants.—The stimulants in common use are *alcohol*, *tea*, *coffee*, and *cocoa*, the last-named deserving to rank among foods. Alcohol is a typical stimulant; it acts as a whip, causing a temporary acceleration of physiological activity. Such acceleration must subsequently be paid for, the extra expenditure brought about by alcohol entailing diminished capacity for further exertion. Alcohol is thus of service only for emergencies of *short* duration; it is eminently harmful when *prolonged* exertion and endurance are required. Like all rapid stimulants, alcohol is in large doses a direct depressant. Tea and coffee owe their stimulating property to the alkaloid *caffein*. They are more useful than alcohol because less liable to abuse, and less dangerous when taken in excess. Cocoa is a stimulant by virtue of *theobromine*, a food by virtue of the large amount of fat or oil which it contains.

The consideration of cost is of great practical importance and not without physiological interest in questions of diet; for the supply-price is a determining factor in the diet scales unconsciously selected by large masses of men, and laid down by the governing authorities of prisons and of charitable institutions.

COMPARATIVE COST OF SOME COMMON FOOD-STUFFS

Food-stuffs	Market prices assumed as the basis of calculation	Number of grammes obtained for one penny	
		of Carbon	of Nitrogen
Milk . . .	2*d*. per pint	20	1·7
Beef . . .	10*d*. per pound	7	1·5
Bread . . .	1½*d*. ,,	80	3·75
Potatoes . .	½*d*. ,,	90	2·7
Oatmeal . .	1¾*d*. ,,	100	5
Dried peas . .	1¼*d*. ,,	110	12
Butter . . .	12*d*. ,,	27	0·06
Eggs . . .	12*d*. per doz.	7·5	1
Rice . . .	1½*d*. per pound	120	2·2
Sugar . . .	1½*d*. ,,	120	—
Cheese . . .	6*d*. ,,	26	4
Cocoa powder .	10*d*. ,,	25	1
Beer . . .	2*d*. per pint	14	0·4

The points which this table teaches or illustrates are: (1) That nitrogen is much more costly than carbon. (2) That carbon in fat is more costly than carbon in starch or sugar. (3) That nitrogen in an animal proteid is more costly than nitrogen in a vegetable proteid.

The table also accounts for the fact that the poorer classes obtain their carbon by sugar rather than by butter, and that, even in the country, milk and eggs rank as luxuries. Beer is recognised to be an extravagance; rice, which is a staple food among oriental nations, and peas, which are a representative article in a vegetarian diet, are particularly economical. And in the prices of the three articles bread, oatmeal, and potatoes, which are most largely consumed by the masses in England, Scotland, and Ireland respectively, we can recognise that the Scotchman gets most for his money, the Irishman least.

According to the now discarded theory of Liebig, proteids were regarded as plastic, fats and carbohydrates as calorific. Bidder and Schmidt considered that only part of the proteid was plastic, and that the remainder was oxidised wastefully, or, as they termed it, that it underwent *luxus combustion*. These views are abandoned; the only sense in which a luxus combustion of proteid can be presumed to occur is by the 'short-cut' conversion alluded to on page 249; and we are about to learn that *all* food is calorific.

ANIMAL HEAT.

Physical data.—*The calorimeter.—Sources of error.—Heat-units.* Amount of heat is measured by the calorimeter, intensity of heat or temperature by the thermometer. Two vessels of water, containing respectively 1 and 2 litres, may be at the same temperature measured in degrees above zero; the first possesses, however, half as much heat as the second, or if the same two vessels of water possess the same amount of heat, then the water in the first vessel must be at a temperature double that of the second. A man weighing 70 kilos possesses twice as much heat as a boy of 35 kilos, the temperature of both being the same, 37°; a fever patient weighing 60 kilos, with a body-temperature of 42°, possesses the same amount of heat as a collapsed person weighing 70 kilos with a body-temperature of 36°.

The unit of heat is the *calorie*, *i.e.* the amount of heat required to raise 1 gramme or cubic centimeter of water 1° centigrade; 10 calories are an amount of heat sufficient to raise 10 grammes of water 1°, or 1 gramme of water 10°, or 5 grammes of water 2°, &c.; thus the amount of water in grammes or cubic centimeters, multiplied by the temperature in degrees, gives the amount of heat in calories. The units of heat further employed to express physiological results are the *kilo-calorie* and the *milli-calorie*, the first being the unit generally used in numbers relating to the total heat-production of animals, the latter that used in the delicate measurements which are made on excised muscles. The kilo-calorie is 1,000 calories, or the amount of heat required to raise one litre or kilo of water 1° ; the milli-calorie is $\frac{1}{1000}$ calorie, or the amount of heat required to raise 1 milligramme of water 1°.

The calorimeter, as used in physiology, is essentially a chamber within which an animal can be confined so as to impart all the heat it produces to a known volume of water contained in a surrounding chamber; an external chamber, packed with non-conducting material, limits as far as possible loss of heat by the water, and the temperature of the latter is read upon thermometers. Let us suppose that the water-chamber contains 10 litres of water, which are raised from 20° to 25°, viz. 5° in one hour by a cat or dog confined in the inner chamber. We know therefrom that the cat or dog has given off 50 calories.

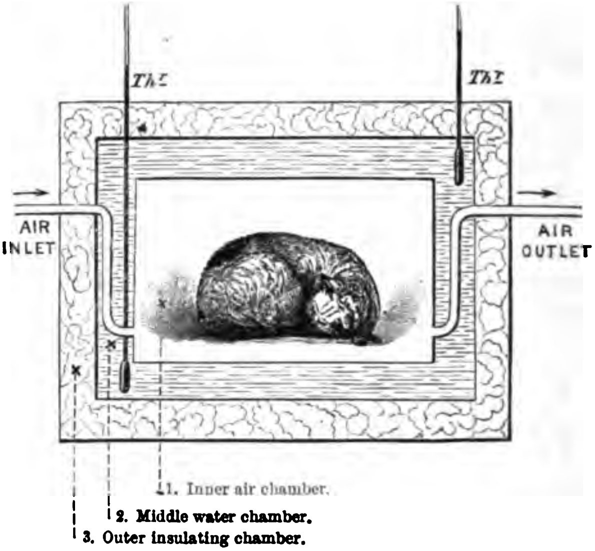


FIG. 103.—CALORIMETER.

Sources of error.—But if the theory is simple, the sources of experimental error are numerous and considerable. It is difficult to determine accurately the mean temperature of a large quantity of water; the material of which the apparatus is constructed absorbs heat; the non-conducting envelope is not a perfect insulator; the temperature of the animal may have risen or fallen; a current of fresh air, which carries off heat and moisture, must be made to enter the chamber. All these circumstances must be taken into account and allowed for as accurately as possible, but it is obvious that a considerable margin of error remains unavoidable.

The **thermometer** is an instrument containing a fluid (usually mercury), which expands by heat. The expansion, and consequently the intensity of the heat which affects it, is measured in degrees, which are the conventional parts into which the total expansion between the freezing and boiling points of water is divided. The scales of degrees in common use are those of Fahrenheit and of Celsius. On the Fahrenheit scale the total expansion is divided into 180 parts or degrees, the freezing point is at 32°, the boiling point at 212°. On the Celsius or centigrade scale the total expansion is divided into 100°, the freezing point is at 0°, the boiling point at 100°.

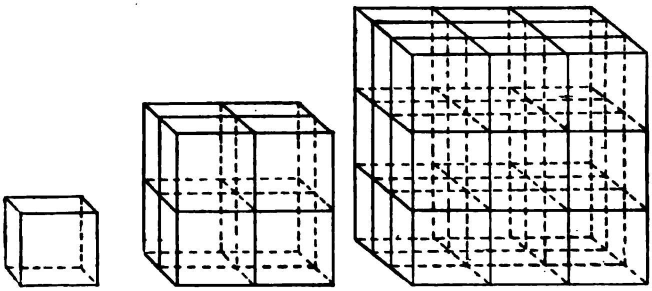


FIG. 104.—DIAGRAM TO ILLUSTRATE THE RELATION BETWEEN VOLUME OR WEIGHT AND SURFACE.

The volumes are . .	1	8	27	&c. cubic centimeters
The weights are . .	1	8	27	&c. grammes
The surfaces are . .	6	24	54	&c. square centimeters
i.e. their ratio of increase is	1	4	9	&c.

Or otherwise, weight or volume increases as the cube, surface increases as the square; or $S = 6 W^{\frac{2}{3}}$.

Mass and surface.—It is important to realise the relation between the weight or mass of a body, and the area of its surface. Animal heat is generated by the substance, lost from the surface, and in the long run gain and loss must balance. But mass and surface do not vary in proportion with each other; the ratio of mass to surface is an increasing one, as may be easily realised in reference to fig. 104 or to fig. 102, giving the approximate body-surface of man from 3 to 70 kilos body-weight.

We thus see that in relation to its weight a small animal has a larger body-surface than a large animal; so that, *ceteris paribus*, a small animal loses heat more rapidly than a large animal; it therefore produces more heat; from which it follows that chemical change must of necessity be more active in a small than in a large animal.

The conclusion is indeed borne out by experiment; weight for weight, small animals produce and give out more heat, more urea, and more CO_2, and consume more food than large animals; and during a given time a larger quantity of blood flows through the tissues of a small than through those of a large animal.

Specific heat capacity.—In the case of animal bodies this may be taken as $\frac{9}{10}$ that of water; *i.e.* an animal requires ·9 kilo-cal. per kilo to raise it 1°, or gives off ·9 kilo-cal. per kilo in falling 1°.

Mechanical equivalent of heat.—Energy cannot be destroyed; it can only be transferred from one place to another. Its various forms are heat, work, chemical action, and electrical action, and it has been experimentally determined how much of one form of energy is equivalent to how much of another form. Thus, it has been determined by Joule that 1 heat-unit is equivalent to 424 work-units. The heat-unit is the calorie; the work-unit is that amount of work required to raise 1 gramme to a height of 1 meter, and is called the grammeter; the kilo-grammeter and the milli-grammeter are its multiples by 1000, and by $\frac{1}{1000}$. Therefore

1 calorie = 424 grammeters.
1 kilo-calorie = 424 kilo-grammeters.
1 milli-calorie = 424 milli-grammeters or 424 gramme-millimeters.

Latent heat of evaporation.—To appreciate the relation between evaporation from the skin, and consequent heat-dissipation from the body, it is necessary to bear in mind the *latent heat* of water, *i.e.* the amount of heat required to convert 1 c.c. of water into water vapour (or *vice versâ*, the amount of heat set free in the transformation from vapour to liquid). This amount varies with temperature, and may under ordinary physiological conditions be taken as 600 calories. It is the amount of heat removed by 1 c.c. of water from the body and from the air in its evaporation. A day's evaporation from the skin and lungs of 1,200 c.c. would require 720 kilo-calories, most of which is drawn from the body.

Animal Heat.—All animals are, as a general rule, warmer than the air or water by which they are surrounded, inasmuch as they are the seat of chemical action. 'Warm-blooded' animals (birds, mammals) exhibit this excess of temperature to a far greater degree than 'cold-blooded' animals (fishes, reptiles, amphibia), and, whereas the temperature of the former varies very little with large variations of the surrounding temperature, that of the latter varies considerably with this circumstance. A man, or dog, or rabbit has a constant temperature, in winter and in summer, at the tropics and in arctic regions;

a frog, or fish, has a low or a high temperature according as the surrounding medium is cold or hot. The warm-blooded animal keeps at a constant temperature by reflex actions of a peculiar character, regulating the heat which is produced in the substance of the body, and the heat which is lost from the surface of the body; the cold-blooded animal has no such regulating power, and, consequently, no fixed or normal body-temperature.

Thermotaxis.—Let us at once look more closely into the manner in which an animal of constant temperature maintains that state. Theoretically, this can be effected in two ways—by variation of the supply, and by variation of the loss—and, as a matter of fact, both these means act concurrently, though the second is the more obviously effective. Heat is supplied by chemical action, and is also in small proportion due to the frictions and concussions which accompany mechanical movements, but these also originate from chemical changes. All chemical actions taking place in the body are originally derived from food, and, as we shall see, the heat-value of the day's food corresponds with the amount of heat *plus* the amount of work given out. More chemical action, more heat; less chemical action, less heat. It has been experimentally shown that in a medium of low temperature a man gives off more carbonic acid than in a medium of high temperature, and it is a matter of common experience that he takes violent exercise to warm himself. These facts are sufficient to prove that the supply of heat is diminished in a hot medium, increased in a cold medium. Heat is dissipated by radiation and by evaporation from the surface of the body; in hot weather the skin is flushed with blood and moist with perspiration, and superfluous clothing is put off; in cold weather the skin is pale and dry, and extra clothing is put on; in the first case the dissipation of heat from the body is accelerated, in the second case it is retarded.

We may in respect of heat regulation compare the body with a room in which heat is generated by a fire, and lost through a window. If it is cold outside, the fire burns high and the window closes; if it is warm outside, the fire burns low and the window opens, and so the temperature of the room remains unaltered in the two cases. The analogy would be drawn closer, and include the manner of heat distribution by the circulating blood, if we considered a room or a building warmed by hot-water-pipes, the water passing through furnaces representing the blood passing through glands and muscles, and the external wall of the room or building representing the skin of the body; the only feature of difference in the two cases is that the hot fluid system is far more minutely ramified in the body than in a building, forming in the former a cutaneous capillary network which is the chief agent of heat dissipation, directly by radiation and indirectly by the maintenance of sudorific action. This cutaneous sheet is the true analogue of the window, and is the principal regulator of body-temperature.

We have seen that at a high temperature a man makes less heat, is comparatively quiescent, has a flushed and perspiring skin, and clothes himself lightly. At a low temperature, he is comparatively active, has a pale dry skin, and clothes himself thickly. In these two opposite states the heat-production and heat-dissipation concur to produce the required correction by varying in opposite senses, viz. *minus* production with *plus* dissipation, *plus* production with *minus* dissipation. It happens otherwise when increased heat is produced simply and solely as the effect of increased tissue activity, *e.g.* by muscular exertion; in this case we have increased production with increased dissipation, and as the result only a slight rise of body-temperature. And if heat-production be diminished, its consequence is a diminution of heat-dissipation, which limits loss of heat and prevents any marked fall of temperature. Thus in these two opposite states the factors concur to maintain constancy of body-temperature by varying in the same sense, viz. *plus* production with *plus* dissipation, *minus* production with *minus* dissipation.

Heat-distribution.—At any given moment the temperature is approximately uniform throughout the body, *i.e.* between 37° and 38°; this uniformity is effected by the circulation of blood, which carries heat to parts where heat is lost, and carries off heat from parts where heat is produced; the blood thus warms cooler parts and cools warmer parts. Within the narrow limits of comparative uniformity, slight differences of temperature are detectable in different parts and in their venous blood, according as such parts are giving or taking heat to or from the blood. The mean temperature of the blood is 38°; the warmest organs of the body are the liver, the brain, and the muscles; the coolest parts of the body are the skin and the extremities. The venous blood returning from the intestines during digestion is warmer than the aortic blood, and becomes warmer still in its passage through the liver. The venous blood of an extremity, although coming from muscle as well as from skin, is as a whole cooler than the arterial blood; the venous blood in the *profunda femoris vein*, which is almost exclusively muscular, is a little warmer than arterial blood (about ·2°). We may illustrate and summarise the thermic relations just discussed, in the following figures selected from various sources, principally from Bernard's observations on dogs, bearing in mind that in this animal the body-temperature is normally somewhat higher than in man.

Average of arterial blood	38 ° C.	
Blood in left ventricle	38·2	
Blood in right ventricle	38·4	
Blood in crural vein	37	
Blood in profunda femoris vein	38·2	
Blood in portal vein	38 to 39	according to the state of digestion
Blood in hepatic vein	38·4 to 39·5	
Brain	40	
Liver	41	
Muscle	38·2 to 39	(relaxed and contracting)
Skin of trunk	35	(or lower)
Skin of extremities	30	„

These are, however, not to be taken as the absolute temperatures discoverable at any one time in a single animal; practically we are restricted to the comparison between any two simultaneous temperatures, and frequently meet with apparent incongruities in the course of successive comparisons; the figures have been selected to exclude these accidental incongruities. And we may call attention to the fact that, although the elevations of temperature are very small, even in the case of glands and muscle, which are the chief heat-producing organs, the absolute heat-production indicated by a small elevation of temperature is very considerable if we take into account the absolute amount of blood passing through the organs; in the case of the liver, for instance, taking the moderate estimate of 500 litres blood per diem raised ½°, we have a daily heat-production of 250 kilo-calories, or one-tenth that of the entire body.

Inflammation.—Brief allusion may be made to the question of heat-production by *inflamed* parts. The name is suggestive of heat-production, but experiments do not justify us in the belief that more heat is produced in an inflamed part, although its temperature is higher than that of a symmetrically placed normal part; the raised temperature is due to vascular dilatation and increased blood-supply, and has never been found to exceed that of arterial blood; to prove that an inflamed part actually produces more heat than usual, it would be necessary to find a temperature of the part or of its venous blood *above* that of the arterial blood, which has not been done.

Nerves and nerve-centres concerned in thermotaxis.—Heat-production, heat-dissipation, and heat-distribution are one and all under control of the nervous system; they further vary together in such a way that a constant body-temperature is maintained. This harmonious and duly co-ordinated action is what we have referred to above as thermotaxis. Proof that *heat-production* is under the control of the nervous system—the temperature of a limb, paralysed by section of its efferent nerves, falls, chemical change is diminished, and the blood which returns through the veins contains less CO_2 than usual. Proof that *heat-dissipation* is controlled by nerves—if a young animal (kitten) is placed in a warm chamber, the vessels of the skin dilate and the paws begin to sweat, changes which do not occur in a limb the nerves of which have been divided. Proof that *heat-distribution* is controlled by nerves—section of a rabbit's sympathetic causes dilatation of the blood-vessels of the ear, and increased temperature; excitation causes the reverse effects.

These are the simplest among many more or less simple cases in which the production, dissipation, and distribution of heat are influenced through nervous channels. The question next arising is whether nerves produce heat variations by an immediate action upon the tissues, or by the intermediation of vascular changes, or as the concomitant of increased chemical change. It is proved that nerves influence the dissipation and distribution of heat by constricting or dilating the vessels which carry the warm fluid, and by exciting or failing to excite the action of the sweat-glands. It is also proved that nerves influence the production of heat by way of the thermal and chemical effects which accompany activity of muscular and glandular tissues. But as regards the direct action of nerves upon heat-production, apart from the vascular and chemical factors, this has never been demonstrated; thermogenic or thermo-inhibitory action of this character is 'unproven,' and must therefore, in default of evidence, be held to be non-existent. Nor have we any experimental right to assume the existence of thermogenic nerve-centres.

Doubtless the nerves which control the three heat processes, by controlling the calibre of blood-vessels and the activity of muscles and glands, are connected with nerve-centres which act and are acted upon by these nerves, and which therefore influence the heat processes. Definite experiments prove this fact; excitation and lesion of particular parts of the brain and cord cause the temperature of the body to vary. But the changes of temperature are dependent upon vascular and chemical changes, and we have no more right to assume the existence of specific thermogenic or thermo-inhibitory centres than we have to assume that of thermogenic nerves or nerve-fibres. Indeed heat-production, unless as the consequence of mechanical or chemical action, is not physically conceivable. This last consideration leads us to recognise that the question of a thermogenic nerve-mechanism is not in reality an independent one, but a part of the much-vexed question of trophic nerves influencing tissue metabolism, which will be considered in a future chapter.

The allusion above made to the influence of particular parts of the brain and cord on body-temperature is founded upon the following observations. Clinical cases are not uncommon of injury to the spinal cord, followed by extremely high temperature; others are met with in which the temperature is subnormal. Experimentally it has been found that punctures of the brain, more especially such as implicate the corpus striatum and optic thalamus, cause a rise of temperature (1° to 2°), which is proved to be due to increased heat-production by direct calorimetry (Richet), as well as by the increased respiratory exchange (Aronsohn and Sachs). Obviously, however, these effects are no proof of the existence of direct *thermogenic* nerve-centres.

The thermal effects which accompany the varying activity of glands are experimentally illustrated by the case of the submaxillary gland of the dog. The temperature of the venous blood and of the saliva is greater during the activity of the gland than during its rest, and it then exceeds that of the carotid blood. The liver affords a still more pronounced instance; the temperature of the hepatic blood is generally higher than that of the portal blood, and the difference is preserved during digestion, when both kinds of blood are raised in temperature.

Normal heat-production of man. Direct estimation.—Direct calorimetrical estimates on man give, as the amount of heat daily produced by a man of average weight, 2,500 kilo-calories, or roughly 100 kilo-calories per hour. It has been found further that the heat-production is least during sleep, greatest during muscular exertion, being approximately—

during sleep	40	kilo-calories per hour.
„ rest	100	„ „
„ moderate movement	150	„ „
„ active exercise	250 to 300	„ „

Indirect estimation.—The heat value of a substance is the amount of heat which is produced by its complete oxidation, and this amount is the same, whether the oxidation be quick or slow, reached by a direct or by a circuitous path; a gramme of sugar or fat burned in a calorimeter, gives the same amount of heat as a gramme of sugar or fat used up by the body. It is, therefore, possible to estimate the amount of heat which must be produced in the body by estimating the heat value of the food daily consumed. In the case of *proteid*, we must take into account that the excreted urea is an incompletely oxidised product, the heat value of which must be subtracted from the heat value of proteid.

The heat value of 1 gramme	proteid	=	5 k. cal.
„ „	fat	=	9·07 „
„ „	starch	=	3·9 „
„ „	urea	=	2·2 „

Therefore in a day's diet—

The heat value of	140	grammes	proteid	=	700	„
„	105	„	fat	=	952	„
„	420	„	carbohydrate	=	1638	„
„	(−*40*	„	*urea*)	=	(−*88*)	
			Total	=	3202	

The amount of heat which the above diet is capable of producing is about 3,200 kilo-calories. The whole of this amount does not, however, manifest itself as such. The animal body is equivalent to a fuel-fed machine; the *total* energy of the food or fuel becomes kinetic in two forms; (1) work of the body or machine, (2) heating of the body or machine; and in the human body the total energy appears in the following proportions—work $\frac{1}{5}$, heat $\frac{4}{5}$. The amount of heat actually generated, and sensible as such, is therefore $\frac{4}{5}$ of 3,200, *i.e.* 2,560 kilo-calories—an amount which is not very different from that obtained by direct calorimetry.

An indirect estimate may also be formed by calculating the heat values of C and H contained in the two chief oxidation products, CO_2 and H_2O. Taking as our data an excretion of 852 grammes CO_2 and 140 grammes H_2O formed in the body, we obtain 1,700 and 500 kilo-calories as the heat values of C and H in these amounts. But this estimate is of little practical value owing to the uncertainty of the H_2O estimate taken as a basis; it is only useful to help us to realise the energy equation of an animal body.

Thermometry—its scope.—By the thermometer we ascertain the temperature of the body, not the amount of heat which it produces or loses. The thermometer gives no measure of the activity of heat-production, nor even any positive indication that it is above or below the normal. This must obviously be so when we reflect that the amount of heat in a given body, and consequently its temperature, is the resultant of two factors—heat-production and heat-dissipation—either or both of which may vary. Theoretically, of course, temperature varies directly with amount of heat produced, and inversely with amount of heat dissipated, but practically the thermometer does not show whether more or less heat is being produced or dissipated. For instance, in *fever*, the body-temperature is usually higher than normal, but we cannot know from this fact alone whether the rise is due to increased production or to diminished dissipation, and it is not surprising that the opinions of authorities have been various on this important point, when reliance has been placed on the thermometer alone.

Enumerating the conditions of which high temperature may be the resultant, we may have any one of the following pairs—normal production with diminished loss; increased production with normal loss; increased production with diminished loss; increased production with increased loss, the former exceeding the latter; diminished production with diminished loss, the latter exceeding the former. Evidently a rise of temperature is not a simple datum; so far is this from being the case that we had better put into tabular form all the various events which may be concealed under a rise or fall or maintenance of body-temperature. And to make the points clearer, we have taken imaginary numbers to illustrate variations of gain and loss, putting the normal at 100—which, if so minded, the reader may take to signify calories per hour. The cases in which 'fever' would be said to exist are indicated by asterisks.

	DATA				CONSEQUENCE
	Heat produced		Heat dissipated		Body-temperature
1	Normal	. 100	Normal	. 100	Normal
2 *	Increased	. 150	Increased	. 150	Normal
2	Diminished	. 50	Diminished	. 50	Normal
4	Normal	. 100	Diminished	. 50	+
5 *	Increased	. 150	Normal	. 100	+
6 *	Increased	. 150	Diminished	. 50	+ +
7 *	Increased	. 150	Increased	. 125	+
8	Diminished	. 75	Diminished	. 50	+
9	Normal	. 100	Increased	. 150	–
10	Diminished	. 50	Normal	. 100	–
11	Diminished	. 50	Increased	. 150	– –
12	Diminished	. 50	Diminished	. 75	–
13 *	Increased	. 125	Increased	. 150	–

It is obvious that from simple thermometric observations no conclusion can legitimately be formed. If the essential phenomenon of *fever* be increased heat-production by increased tissue metabolism, then it is obvious that there may be fever with a body-temperature above, at, or below normal, and as a matter of fact it is admitted by all reliable clinical authorities that the febrile process may be intense when body-temperature is normal or even low.

It would be a valuable supplement to our precise knowledge of fever in its different stages if, failing the calorimeter which cannot be used clinically, thermometric indications were supplemented by systematic readings of expired CO_2; these give measure of tissue change, and are obtainable—not, indeed, without great care—but without great practical difficulty.

If the reasoning above given has been properly followed, it is obvious why the important and apparently simple question—'Is the increased body-temperature of fever the result of increased heat-production, or of diminished heat-dissipation (=heat-retention), or of both factors?' has not even now, with the aid of calorimetry and thermometry combined, received its final and assured answer. We may only say that it is highly probable that both factors come into effect at different periods of a febrile attack.

Considered from the experimental side the possibilities exhibited in the table show that great caution is necessary in drawing conclusions, even from calorimetrical observations on animals. By the calorimeter we read heat-dissipation, and infer heat-production; a larger calorimeter reading with a *falling* body-temperature is bad evidence of increased heat-production; to be good evidence it must occur with a constant, or better still with a rising body-temperature. A smaller calorimeter reading with a rising body-temperature signifies heat-retention; to be good evidence of diminished heat-production, it must occur with a constant, or better with a falling temperature.

Surface temperature and deep temperature.—It is hardly possible to employ calorimetry for clinical study, but with a due appreciation of the relation which must obtain between temperatures of the surface and of internal parts, it is possible to use the combined data for an approximate estimate of any very considerable alterations of heat-production or of heat-dissipation. To make the matter clear, we may consider the two conceivable extremes by which a febrile temperature of the body may be produced, 1, an abnormal heat-production; 2, an abnormal heat-retention. In both cases the internal temperature will be high, but in the first case the surface temperature will be higher than in the second. The method of taking a surface temperature is of some importance; it is not possible to obtain an *absolute* surface temperature, for the instrument applied to the skin protects the subjacent area, and causes its temperature to approximate more and more towards that of deeper parts; but as the information desired is 'how quickly is the skin giving off heat,' this difficulty is avoided by using the thermometer as a thermoscope, reading the rise which is produced from a given starting point (20°) during a given period (½ min.); we thus obtain an indication of the 'heat tension' of the cutaneous surface. To complete the estimate it would be necessary to take into account the rate at which the evaporation is taking place by the lungs and skin.

Simple clinical thermometry, although from a physiological point of view yielding very complex results, is nevertheless of great practical value, if carefully performed with reliable instruments, and not committed to the charge of careless assistants. Taken with other indications the temperature is valuable evidence of the presence and degree of fever, and of its probable course. But, to be of use, the observation should be taken twice or four times in the twenty-four hours, and entered for reference upon a temperature chart. The graphic curve of several days is of far more value than a single isolated observation. In view of startling statements occasionally made, it is not superfluous to mention that clinical thermometers should possess an index in working order, that the index should be shaken to below the normal point before use, that any suspected instrument should be reverified, and finally that a malingerer may know how to send a thermometer to fever-point by rubbing it against the blankets. Other memoranda are, the normal daily fluctuations of temperature, the effect of digestion, and of exercise, the variations with sex and age. Normally, temperature rises during the day and falls during the night, being thus at its highest at the end of the day, at its lowest at the end of the night. Normally, again, the temperature is raised after a meal, and after exertion—more so, indeed, on a weak than on a healthy subject. Finally, the temperature is less constant in women than in men, and least constant in children. A high temperature is as a rule more significant in a man than in a woman, and in a child it may possibly signify nothing more than a recent fit of crying. The part selected for thermometry may also influence the result; in the axilla the normal reading is 37°, in the mouth 37·2°, in the rectum 37·6°, and the last-named is the most trustworthy of the three temperatures.

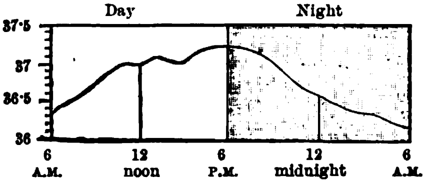


FIG. 105.—NORMAL TEMPERATURE CHART OF THE HUMAN BODY DURING THE TWENTY-FOUR HOURS.

After an animal has been killed its body-temperature does not at once begin to fall, like that of an inert mass which has been heated to the same degree. The internal temperature may even rise after death, because with arrest of the circulation and respiration, loss of heat has been arrested, or at any rate greatly diminished, while the organs and tissues have still continued to produce heat. This *post-mortem* rise is not solely attributable to rigor mortis, for it makes its appearance sooner; it is a manifestation of the residual metabolism of the tissues and organs of the body, and an expression of the fact that their death does not coincide with that of the organism—the individuals outlast for a time the dissolution of the community. No doubt muscle takes a chief share in such effect, and in so far as it does so, its rigor must contribute to delayed cooling; we find, moreover, that in cases where rigidity appears early and strongly (*e.g.* tetanus) the *post-mortem* rise and the delayed fall of temperature are most pronounced. But even in such cases rigor is not the sole factor, it is only one factor in the general tissue vivacity of which it is a sign. On the other hand, if death supervenes as the termination of chronic disease, if at the death of the body the tissues are moribund, there is no *post-mortem* rise of temperature, and the cooling of the body is but little delayed in comparison with that of an inert mass. Deaths from fever afford instructive illustration of the varying thermic effects of residual metabolism; the tissues of a fever patient dying at a high temperature are active, and by continuing active retard the cooling of the body after death; the tissues of a fever patient dying at a low temperature are already moribund, and have but little retarding effect upon the further cooling of the body.

PART II

THE PHENOMENA OF EXCITATION

CHAPTER VIII

GENERAL PLAN OF THE NERVOUS SYSTEM

PAGE
290 **Excitability—The reflex arc—Reflex action.**
293 **Cortical and medullary centres—Brain, bulb, and cord—Voluntary (automatic) and reflex acts—'Master' centres and 'foreman' centres.**
300 ***Why* and *How*?**

PROTOPLASM is excitable. When any part of a lump of protoplasm is excited, the lump moves. When many lumps of protoplasm are gathered into a homogeneous mass, excitations and movements may be transmitted from lump to lump in all directions. With higher organisation of the mass, differences of function and of structure begin to make their appearance. Excitability, while still pervading the whole organism, becomes localised with greater intensity in some parts than in others, along some lines more than along others (sense-organs, nerves, and nerve-centres) ; in other parts contractility becomes the salient character (muscles). To illustrate this progressive elaboration of a nervous system we may select—(1) an amœba, (2) a jelly-fish or a hydra, (3) a frog, (4) a man.

An amœba is a simple lump of protoplasm, excitable and contractile in all parts of its substance, and not more so or less so in one part than in another.

The lower surface of the umbrella of a jelly-fish is covered with a layer of contractile protoplasm which is not far removed from a homogeneous state; an excitation applied to any part causes a contraction which is transmitted in all directions through the mass; it is a sheet with neuro-muscular properties, a network of rudimentary muscle and nerve. A fresh-water hydra supplies us with another good instance of commencing differences of structure. The contraction of which it is capable is localised in a contractile network formed by the processes of certain neuro-muscular cells, which are excitable though not themselves contractile.

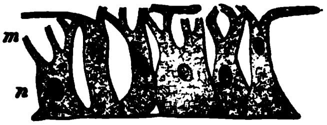


FIG. 106.—NEURO-MUSCULAR CELLS. (Gegenbaur.)

A frog exhibits a far higher degree of differentiation. Instead of a neuro-muscular cell we have a comparatively complex chain of parts different in structure and in function, muscle-fibre exhibiting contractility as its salient characteristic, nerve-fibre and nerve-cell possessing conductivity without contractility. In such an animal we recognise the component parts of a nervous system as central, peripheral, and intermediate, and, as we shall see, we may further analyse these components into cerebral and spinal centres, into afferent and efferent conductors, and into many kinds of end organs in connection with these conductors.

The progressive elaboration of a nervous system with subdivision of function has its highest expression in the human brain. There is in the human brain, and in less degree, as we go down the scale, in the mammalian brain, a localisation of different functions in different parts. We shall find that this localisation is best known in the cases of language, of voluntary motion, and of sight, and that as regards voluntary motion in particular, it is possible to trace a correspondence between particular movements and the functional activity of particular areæ of the cerebral cortex.

The literal meaning of the word ex-citation is 'call from without.' The surroundings of an organism *excite* its specially excitable parts, and the organism moves to or from its surroundings, or registers an impression which will modify its future movements. The specially excitable parts are on the external surface, exposed to excitation: they have no direct communication with the specially contractile parts—the muscles; but an indirect communication by strands of specially excitable protoplasm—nerve-fibres, which conduct excitations to central organs where they are received, while other nerve-fibres establish the communication from the nerve-centres to the muscles, conducting from the former to the latter the impulses which give rise to movements.

The central nervous cell is usually considered as a double cell, one part of which is at the central end of an afferent fibre, the other half of which is at the central end of an efferent fibre. The first is called a *sensory* cell, the second is called a *motor* cell; and we must imagine that a bond of union (commissural fibre or fibrils) establishes communication from 'sensory' to motor cell (but see p. 533).

The component parts just enumerated form a reflex arc, and may be classified as central, peripheral, and intermediate. The central part is a nerve-centre or centres, the peripheral parts are the sensificatory organs and the muscles, the intermediate parts are the nerves—afferent and efferent—and the fundamental nervous act is a reflex act. In relation to the conduct of the animal body, the sense organs are the intelligence department, nerve-centres are the headquarters, muscles are the executive, nerves are the channels of communication.

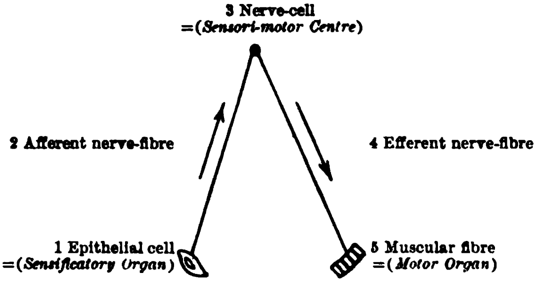


FIG. 107.

In the ascending scale of organisation there is increasing diversity of parts, increasing subdivision of properties and of functions, with further diversities between the parts of parts. The simple nervous system above figured is not that of a mammalian animal nor of man. The 'nerve-centre' of mammalia and of man is a collection of nerve-centres occupying the cerebro-spinal axis, with more or less diverse special offices under their control—communicating each with the other upon occasions, yet separately active upon other occasions—having functions which are localised at certain parts, yet not strictly confined to these parts—playing upon and influencing each other in all directions, yet in some directions rather than in others, and maintaining some kind of precedence and rank, so that while all may influence all, yet some are usually guided and controlled by others—variously organised through past excitations, yet still variously organisable by excitations to come. To-day the state and disposition of organs and of the organism are the product of the past, immediate and remote, individual and ancestral. To-morrow and in the distant future they will become what they may be made to become by training, by education, and by new conditions of life.

Classification of nerve-centres.—The cerebro-spinal centres may for convenience be classified as: (1) cerebral or cortical; (2) spinal or medullary; and the reactions of these two classes may be characterised as (1) voluntary; (2) reflex.

Intermediate between these two classes, partly including both, and absolutely distinguishable from neither, a third class of central action may be recognised—characterised as *automatic* action; in view of the confusion of thought which has often arisen from the use of this word, it would perhaps be better to avoid it altogether; at any rate we must define the sense in which it is to be employed. The word has received two diametrically opposed meanings, viz. (1) self-moving, self-arising, spontaneous, in literal translation of αὐτό-ματος; (2) automaton-like, that is to say, like a mechanism which appears to be self-moving, but which we know to be moved by secret springs and hidden keys. The second sense is that in which the word is used in this book. When we attempt to distinguish the characteristics of an automatic from those of a voluntary or of a reflex action, we find that the automatic action is one which at first sight appears to be voluntary, which is usually performed unconsciously, and that an exciting cause of the action, although not obvious, is nevertheless discoverable. In fact, the automatic action is essentially a reflex action, and differs from it only in that it is as a rule the habitual or serial effect of habitual or serial stimuli; *e.g.* walking, mastication, respiration, &c. Although the word is in certain respects a convenient one to use, if properly guarded by definition, we do not see reason for applying it as a classifying term on the same footing as the terms *reflex* and *voluntary*, and shall employ it as a subordinate term for certain habitual actions belonging to voluntary or to the reflex categories.

An automatic act is the repeated or rhythmic motor response to a repeated or continuous excitation. Usually it is carried on unconsciously, but it may upon occasion be attended to, and its effects felt, and it may be accelerated or restrained by voluntary action. The movements of respiration, of sucking, and of walking, are the most typical among automatic actions; each of these actions is a more or less prolonged and rhythmic series of motor responses to prolonged or repeated excitation. In the case of breathing, the rhythmic series of movements lasts through life, its chief excitant being the state of the blood acting upon the spinal medulla. The automatic act of walking is carried on in the form of more or less prolonged series of movements subject to voluntary control, consciously or unconsciously, but generally unconsciously, and in response to the series of excitations caused by contact with the ground and state of muscular tension. Skilled movements such as writing or speaking are on the border-land between automatic and voluntary; they began as voluntary, and they have later become automatic: even in its fully-developed form each such automatic series of movements is initiated by voluntary effort, and in its highest manifestations is effected in largest measure with the participation of voluntary cerebral action.

Reflex action.—We may define a *reflex act* as the *immediate* motor response to centripetal excitation; it is unchosen, 'fatal.' It is subserved by:—

1. Epithelium (peripheral sense-organ).
2. Afferent nerve-fibre.
3. Spinal cell upon afferent tract.
4. Commissural fibre.
5. Spinal cell on efferent tract.
6. Efferent nerve-fibre.
7. Muscle (peripheral motor-organ).

If the peripheral excitation is weak, a reflex act may be inhibited. If the peripheral excitation is strong, the act may be performed in spite of an inhibitory effort. It may be performed unconsciously, and never be known to its performer, or it may be unconsciously performed, and become known subsequently, or it may be perceived during its performance.

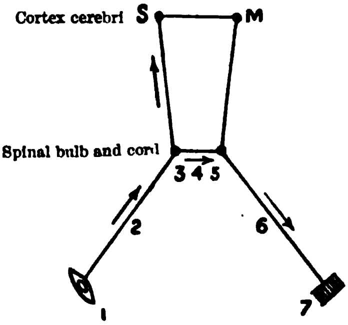


FIG. 108.—REFLEX ACTION.

These several modes and possibilities will be best appreciated by considering examples of each as they occur in everyday life. The most undeniable of reflex acts are those of a paraplegic patient or of a headless frog, when in response to cutaneous stimulation the limbs move. The act of winking in response to an irritation of the conjunctiva, or to retinal stimulation, caused by the sudden approach of a missile, is likewise a reflex act. By a voluntary effort the act of winking may be restrained—inhibited; but it may happen that the irritation becomes so irresistible, or that a threatening blow is so sudden, that no voluntary effort can restrain the act; it is a familiar experience with most people that the eyes are continually winking without consciousness having been aroused, and that by paying attention to the matter they may become conscious of the act. Sneezing and coughing, although more complicated, are to be classed among typical reflex actions; a person may sneeze or cough unconsciously or consciously; he may or he may not be able to restrain a sneeze or cough; he may have sneezed or coughed unconsciously at one time, and yet may subsequently remember the fact, and may then become conscious of having sneezed or coughed.

All the foregoing instances are typical reflex actions, in the performance of which the spinal bulb and spinal cord are the organs of 'return of action.' But the term 'reflex action' has spread beyond these its original limits, and as commonly used at the present day. embraces on the one hand the reactions of visceral muscle and of gland tissue in which the spinal cord is the centre of return of action, and on the other hand includes many highly complex series of movements in which the bulb or even the cerebral cortex takes a leading part, but which may nevertheless be carried on with or without the participation of consciousness. Instances of the reflex action of visceral muscle are furnished by the modifications of the heart's beat, and of the state of the blood-vessels, which are brought about by centripetal stimuli acting through the spinal bulb and cord, and giving rise to centrifugal impulses along vaso-augmentor or vaso-inhibitory nerves. Of this class of reflex effects, blushing or pallor, fainting or palpitation are the most familiar instances. It is to be noted that in this, more than in any other class, the reflex effect can most obviously be of two kinds, a reflex increase of action or a reflex diminution of action. Reflex contraction of smooth muscle is also exemplified in the third stage of deglutition, in the act of defæcation, in the case of the urinary and biliary bladders, and in the alterations of the iris consequent upon optical stimuli. Reflex glandular action is well characterised in the case of the salivary and lachrymal glands by the effects which are produced by excitation of the mucous membrane of the mouth or of the orbit.

Turning to the consideration of reflex acts in which the bulb or brain are undoubtedly organs of 'return of action,' we recognise that we have reached to, if not beyond, the furthest limit of the term reflex. Walking, breathing, sucking, skilled movements such as those of an accomplished dancer or musician, acts unconsciously performed but bearing all the marks of intelligent purpose, the unconscious cerebration of a mathematician or of a poet, all these are not unfrequently called reflex and alluded to as reflex actions; 'automatic,' in the sense of 'automaton-like,' as defined above, is the more correct qualification to use, although, if we bear in mind that the term 'automatic' is in reality covered by the term reflex (an automatic act being an habitual or serial reflex), it is not absolutely incorrect to call the actions reflex. But it is better to distinguish the group of automatic actions out of the larger class of reflex actions and to refer to them under that designation. These automatic actions are distinguishable into two sub-groups, (1) the primary or inherited automatic acts already considered, (2) the secondary or acquired automatic acts. Respiration is a primary automatic act; writing is a secondary automatic act. Walking occupies a position midway between the primary and secondary groups; it is primary in so far as the disposition to walk is inherited; it is secondary in so far as a child must learn to walk by practice.

Voluntary action.—To anyone who will reflect upon the three words, reflex, automatic, voluntary, it will be evident that the actions so qualified overlap, and that the words themselves can only be arbitrarily defined. We have recognised automatic to belong to reflex action; we shall find that, subjectively viewed, *i.e.* by appealing to our own self-consciousness, we all believe our voluntary actions to be spontaneous and freely chosen in spite of exciting impulses; objectively viewed in the conduct of living beings as it unfolds itself before us, voluntary action appears as a highly disguised and complicated form of reflex action, with its causal excitations more or less concealed, more or less deeply buried in the past history of the individual, or of the ancestors. From either point of view, it is most difficult to settle upon a satisfactory *differentia* by which to characterise and identify a voluntary action. But this is not to say that voluntary is to be entirely undistinguished from reflex action. On the contrary, the difficulty having been clearly realised, may be, if not logically surmounted, practically turned, by careful description of typical reflex, and of typical voluntary actions. As voluntary actions of the highest order we may instance the working out of a mathematical problem, the opinion uttered by counsel or by physician, the composition of a picture or of an opera, the directions pronounced by a responsible leader. From actions of this order, down to the aimless saunterings of an unemployed person, bent in this or that direction by each trivial incident, the movements of apparently free agents are termed voluntary. No line of demarcation can be drawn anywhere between the more or less voluntary actions included between these two extremes. But on review of the whole scale we recognise that an act is voluntary and cerebral in proportion with the imagination and judgment which intervene between sensation and motion. A single voluntary contraction, a shorter or longer series of voluntary contractions, the life-long pursuit of a policy, alike imply the following elements—(1) the consciousness of a desire, *i.e.* sensation; (2) comparison and deliberation of cerebral ideas, *i.e.* judgment; (3) executive action, *i.e.* voluntary motion.

Nor is it possible to lay down at any point a boundary line between the highest voluntary and the lowest reflex action; the quality of centre, whether of brain or spinal cord, is the resultant of past impressions—individual and ancestral, and upon that quality depends the motor result of each given centripetal impulse and sensation. Contrasting the two extremes, we have in the purest reflex action an immediate, 'fatal,' unchosen response to peripheral stimulation; the nervous path is deeply canalised; alternative reactions are few, the particular reaction to a particular stimulus is easily predicted. In the purest voluntary action we have a delayed, 'free,' chosen response to a given sensation; the nervous path is not preformed; alternative reactions are numerous; the particular reaction to a particular sensation cannot be predicted. Between these extremes all imaginable movements and actions of men and of animals find their place.

From the objective point of view of the observer and experimenter, the most definite *differentia* between reflex, automatic and voluntary actions is afforded by the time factor. A *reflex* act is a single *immediate* motor reaction; an *automatic* action is a *series* of immediate motor reactions; *voluntary* action is *delayed* motor reaction.

If the doctrine of spontaneous volition be accepted (an admission which seems to entail acceptance of the view that effects may occur without causes, or phenomena without generators), the voluntary act commences at the cortical motor cell. But it is more logical to admit that previous sensations have been registered, and that volition is a resultant of past as well as of present sensations. The cerebral sequence is to feel, to judge, to will, and the principal characteristic of cerebral action is great *delay* of reaction, in contrast with the immediate response characteristic of reflex acts.

A voluntary act is subserved by :—

1. Epithelium.
2. Afferent nerve-fibre.
3. Spinal sensory cell.
4. Afferent tract.
5. Cortical sensory cell.
6. Commissural fibre.
7. Cortical motor cell.
8. Efferent tract.
9. Spinal motor cell.
10. Efferent nerve-fibre.
11. Muscle.

A cerebral act is usually attended by consciousness, but undoubted cerebral acts may be unconsciously performed. A cerebral act is usually voluntary, *i.e.* chosen, but it may be automatic or reflex, *i.e.* an immediate and involuntary response to peripheral excitation, either as a single action, or as a prolonged series of acts.

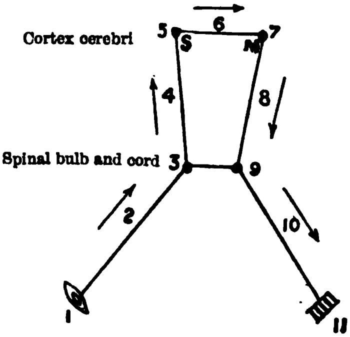


FIG. 109.—VOLUNTARY ACTION.

A familiar comparison may serve to bring home to some minds a clearer picture of the relation which subsists between cerebral and spinal shares in the government of the body, and lead to a rational conception of the relative significance of the terms voluntary and reflex. An ordinary business enterprise, a factory, a political party, an army—in short, any body of men gathered together under leadership—is like the collection of cells forming the animal body, led and controlled by certain individuals whom we may call nerve-centres, and characterise as 'master centres' and as 'foreman centres.' The function of a master centre in a body, as in a business, is mainly that of administration, to initiate proceedings the detailed supervision of which is delegated to and carried out by foreman centres, to actually take part in supervision only of novel proceedings or of proceedings which go awry; the function of a foreman centre is mainly that of immediate supervision, to execute instructions received from the master centre, to issue instructions in matters of routine without reference to headquarters, but to inform and take instructions from the master centre as emergence arises. This is a true picture of the relations between the cortex cerebri and the medulla spinalis, as far as we know or can conceive them.

The analogy might easily be pushed further, but analogies are to be used with caution; it is, however, allowable to point out (1) that while the mandatory and inhibitory intervention of superior centres is necessary at times, attempts at detailed interference with reactions which are normally within the province of subordinate centres, would embarrass smooth working. Thus a man who should attempt to walk or write by a series of voluntary movements would walk badly, or write badly. (2) That although most experimental evidence is to the effect that those functions which we may regard as the domestic concerns of the body—circulation, respiration, secretion—are regulated by subordinate centres, by the grey matter of the spinal bulb and cord, yet we must recognise from pathological evidence, and from some few physiological experiments, that the cerebrum may, upon occasion, take cognisance of the domestic state as well as take part in its regulation or in its disarrangement.

We may in conclusion take this opportunity of pointing out that the relative importance of cerebral and spinal control varies with rank in the animal scale. As we ascend in the scale the importance of the cerebrum increases, that of the spinal axis decreases. The importance of cerebral function is greater, that of spinal function is smaller, in a dog than in a frog, in a man than in a dog. The range and variety of cerebral action increase, whereas the range and variety of spinal action decrease as we ascend in the animal scale. Although the entire cerebrospinal conduct is more fixed and stereotyped in a frog than in a dog, in a dog than in a man, the increased freedom and variety do not include spinal but only cerebral action; spinal reactions are more limited and stereotyped in man than in the dog, in the dog than in the frog.

The considerations conveyed in the preceding pages may now be summarised as follows:

Adjustment of the organism to the environment *Reflex action* in the broadest sense of the word	BRAIN *Voluntary action* (*i.e.* deliberately chosen)	Secondary or acquired properties	Regulation of external affairs, or functions of relation	Cerebro-spinal control
		Primary or inherited properties		
	BULB *Automatic action* (*i.e.* automaton-like serial reflex movements)	Secondary or acquired properties		
	CORD *Reflex action* (in the original and limited sense of the word)	Primary or inherited properties	Regulation of internal affairs, or functions of nutrition	
		Organic properties		

It is necessary, in order to define the scope of the foregoing analysis, to add a few words of limitation. We have followed an idea to the borderland of physical phenomena which can be measured by our senses. We have glanced across the limit into regions where questions and opinions cannot be measured by objective means, although they have been fearlessly broached and freely pronounced upon by schoolmen and by churchmen. We desire not to trespass upon those regions. The question *why*? is not answered by positive science, but only the question *how*? and sometimes the question *how much*? Physiological problems are limited to the tangible and measurable phenomena of living bodies. The physiologist cannot say why a muscle contracts, nor define 'life,' 'free will,' 'moral responsibility;' his professed task is limited to an objective study of the essential particulars in which living differs from inert or dead matter; he can learn 'how' a muscle contracts, under what conditions, how much, and with what effects; the original cause of the property termed contractility is beyond his knowledge.

The distinction just drawn is of fundamental importance; it should be emphasised and clearly apprehended that the choice open to us often lies between these two paths: between a vain attempt to answer the question *why*? to discover a final cause 'a quo' or a final cause 'ad quem': and the feasible task of studying relations between phenomena, of retracing successive steps of 'how' in the procession of events. We may be able to see how things have happened or will happen, we have no right to say why they have happened, or why they will happen; and it is a first step in the acquisition of positive knowledge to know that the '*ràtio rei*' is not the 'reason why.'

In the review of the nervous system upon which we are entering, we shall describe the physiological properties or *modus vivendi* (1) of the peripheral organs—muscle and nerve—(2) of the sense organs—eye, ear, &c.—(3) of the central organs—spinal cord, spinal bulb, and brain. Animal electricity, although a general phenomenon of chemical change, will, on account of its close association with excitation effects, be considered in connection with muscle and nerve; on the other hand, several subjects belonging properly to the nervous system, *e.g.* the larynx, vascular nerves, &c., have already, of necessity or for convenience, received attention in Part I.

CHAPTER IX

MUSCLE

PAGE * ELECTRO-PHYSIOLOGICAL INSTRUMENTS

302 **Daniell cell:** Anode and kathode—Du Bois-Reymond's key—Pohl's commutator—Ohm's law—Potential—Resistance—Current—Electrical units—Rheostat—Rheochord—Wheatstone bridge—Current-diffusion — Distribution of potential.

309 **The galvanometer:** Of high resistance—Of low resistance—Compensation—Unpolarisable electrodes—The Rheotome.

313 **Thermo-electric measurements.**

314 **Lippmann's capillary electrometer.**

315 **Du Bois-Reymond's induction coil:** Single shocks—Faradisation—The Helmholtz side-wire.

317 Electrical Chronographs.

MUSCLE.

318 Smooth, striated, and cardiac – Red and pale striated—Motor end-plates and ganglionic networks.

318 **Histological characters:** Of resting, of contracted, and of rigid muscle.

320 **Chemical composition of muscle:** Its alterations in rigor and by activity—Muscle-plasma, myosin, and muscle-serum—Their preparation – Sarcolactic acid—Carbon dioxide—Differences between fatigued and rested muscle—Extractives.

323 **The properties of muscle**—*Physical*: Extensibility and elasticity—Viscosity—*Physiological*: Excitability or contractility.

325 **Contractility:** Stimuli, direct and indirect, maximal and minimal—The wave of contraction—Constant current—Induced current.

329 **Myographs:** A single contraction—Summation of contractions—Clonus—Tetanus—Load and after-load—Isotonic and isometric curves—Variations of contraction with kind of muscle, fatigue, and temperature.

335 The muscle sound—Nature of voluntary contraction—of cardiac contraction—Absolute strength—Work—The three levers—Co-operative antagonism—Heat.

343 **Curare.**

THE peripheral nervous system is composed of nerve-fibres and their terminations, and also includes a large proportion of nerve-cells, which enter into the constitution of ganglia and ganglionic plexuses. The peripheral terminations of nerves fall into two chief classes, sensory and motor; the sensory being mainly distributed on the external surface of the body, in the skin and sense organs; the motor, in the voluntary skeletal muscles. Muscles may indeed properly be regarded as the end-organs of motor nerves, and it is in many respects convenient to consider the physiology of muscle in conjunction with that of nerve. Their experimental study necessitates the use of certain electrical instruments and a knowledge of the physical principles involved. These data are therefore presented in their natural place as the physical preface to the physiology of the nervous system.

ELECTRO-PHYSIOLOGICAL INSTRUMENTS AND PRINCIPLES

The **Daniell cell** is the type of all other cells in common use; it consists of two elements, zinc and copper, and of two fluids, H_2SO_4 and $CuSO_4$, separated by a porous septum. The positive element, at which most chemical action takes place, is the zinc, which dips in the sulphuric acid contained in the porous pot; the negative element is the copper, which dips in the copper sulphate solution. The end of the wire connected with the zinc is the *negative electrode* or *kathode*; that connected with the copper is the *positive electrode* or *anode*. The copper sulphate solution should be saturated, and kept so during use, by an excess of the salt; the zinc should be amalgamated before use in order to prevent its waste by local action; and when a Daniell cell is required to supply a current of constant strength, it is well to substitute a saturated solution of zinc sulphate for the sulphuric acid in the porous pot. The direction of current throughout any circuit is from positive to negative—from higher level to lower level; *e.g.* in a circuit composed of a Daniell cell and of wires leading to a nerve laid across electrodes, the direction of current in the cell is from zinc, the positive element, to copper, the negative element; outside the cell, it is from the copper to the anode, through the nerve from the anode to the kathode, and from the kathode to the zinc. As regards the nerve, the anode, or positive electrode, is the seat of entrance of current; the kathode, or negative electrode, is its seat of exit.

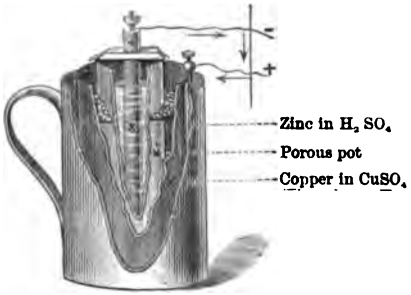
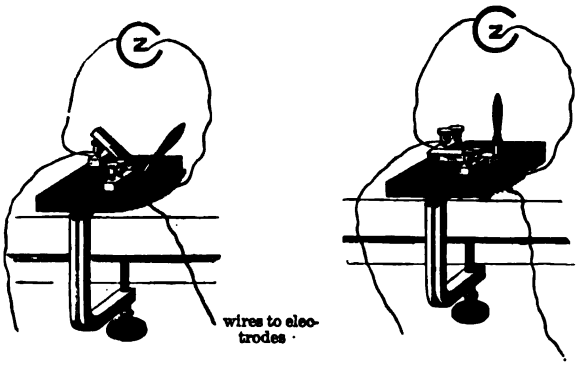


FIG. 110.—DANIEL CELL REPRESENTED SO AS TO EXHIBIT ITS CONSTITUENT PARTS.

Keys and commutators of various patterns are used for conveniently making and breaking a current, and for reversing its direction. A key in common use is the *Du Bois-Reymond* key, which consists of two metal blocks, each carrying two binding screws, and joinable at will by a third metal piece which is raised or lowered by a handle. This key can be used in either of two ways : (1) the key can be interposed in one wire of a cell, in which case the circuit is *made* by lowering the junction piece, and *broken* by raising it ; (2) both wires can be brought to each side of the key, from which two other wires lead off to the electrodes ; in this case the circuit through the electrodes is *broken* by lowering the junction piece and *made* by raising it.



Key open ; current passes to electrodes.

Key shut ; current passes through key.

FIG. 111.—DU BOIS-REYMOND'S FRICTION KEY.

Put up so as to 'short-circuit' current when it is closed.

The commutator generally used in a physiological laboratory is *Pohl's mercury commutator*, the construction of which is as follows. A block of insulating material (ebonite or paraffin) is provided with six pits containing mercury, with which six binding screws fixed in the block are in communication. Two cross wires establish junction between the pools of mercury, as shown in the figure. A cradle consisting of an insulating handle fixed to two metal arcs, can be tilted so that each of the two middle pools can at will be brought into communication with either of the two lateral pairs of pools, right or left. Wires are connected with the middle pair of pools and with one of the lateral pairs.

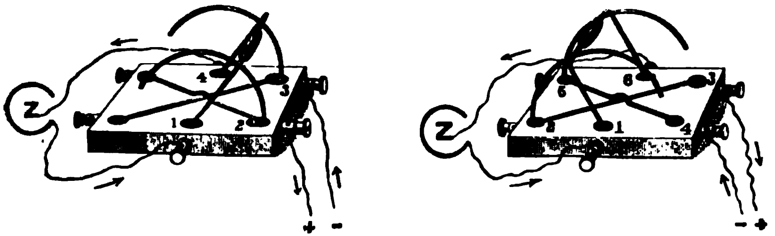


FIG. 112.—POHL'S COMMUTATOR (WITH CROSS WIRES).

The Daniell cell and electrode wires remaining fixed, the direction of current in the latter is reversed by moving the cradle to right or left. Numbers 1, 2, 3, &c. indicate the path of current in the two cases.

Tilting the cradle to right or left reverses current through an electrode circuit, as can be seen by tracing its path in the figure, or better, by putting up a circuit consisting of a Daniell cell, key, commutator, and galvanoscope.

A commutator is often used for a different purpose without the cross wires. In this case both battery wires are connected with the middle pools, two other pairs of wires connected with the two lateral pairs of pools leading off to two pairs of electrodes, which can be applied to two portions of a nerve, or to a nerve and to a muscle. By tilting the cradle to right or left the battery current can now be turned on to one or other pair of electrodes (see fig. 181).

A comprehension of the meaning of *Ohm's law*, and of the terms *current*, *resistance*, *electromotive force*, *potential*, is an indispensable preliminary to the study of electro-physiology. These terms can be sufficiently explained by comparing an electric current with a current of water, although the analogy is in some respects defective. An electric current from a Daniell cell flows through a wire from positive to negative potential, just as the water from a raised reservoir flows through a pipe from higher to lower level. Potential remaining constant, more current flows through a thick than through a thin wire, just as, water pressure remaining constant, more water flows through a broad than through a narrow pipe. A thin wire offers a greater resistance to the passage of current than a thick wire, just as a narrow pipe may be considered to offer greater resistance than a broad pipe. With a given wire there is more current from higher potential, just as with a given pipe there is more current from a higher water-level. The driving force is called electro-motive force, electro-motive difference of potential, potential, or pressure; these are synonymous terms, and the last—viz. pressure—brings out clearly enough the analogy of electrical potential or pressure with water-level or pressure.

Ohm's law is simply a short formula embodying the above considerations, viz. $C=\frac{E}{R}$, or amount of current varies directly as electromotive pressure, and inversely as resistance. We are already familiar with an analogous but less simple and precise relation in the physics of blood-flow, to the effect that amount of flow increases with increased heart's force, diminishes with increased peripheral resistance. An electrical current can be increased by increasing the electrical pressure, or by diminishing the resistance; it can be diminished by diminishing the pressure, or by increasing the resistance. The principle of electrical measuring instruments may also be understood by comparing them with instruments already familiar to the student of physiology. Amount of blood-flow is ascertained by calculation from the indications of a stromuhr, or current-clock. Amount of electrical flow is ascertained from the indications of a **galvanometer**. Blood-pressure is measured by a manometer; potential or electrical pressure is measured by an **electrometer**, which is practically an electrical manometer.

The conventional names given to the electrical units we employ in physiology are as follows:—

The unit of current is called an **ampère**.

The unit of resistance is called an **ohm**.

The unit of pressure is called a **volt**.

The potential or pressure of a Daniell cell is nearly one volt, the internal resistance of an ordinary cell ranges from $\frac{1}{2}$ to 10 ohms. 1 volt *pressure* through 1 ohm *resistance* gives 1 ampère *current*; through 10 ohms, it gives $\frac{1}{10}$th ampère, &c.

A **rheostat** is a set of resistance coils graduated in ohms, by means of which more or less resistance can at will be put into a circuit.

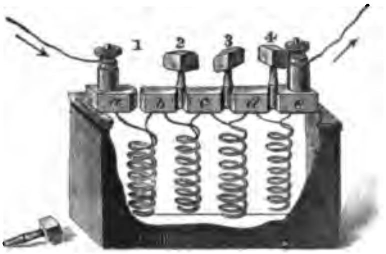


FIG. 113.—RHEOSTAT.

Wires of definite resistance unite the metal blocks *a b c d e*, which can be connected and disconnected by inserting or removing metal plugs. If all the plugs are inserted, the resistance is practically zero; if a plug is removed (as shown in figure), resistance in a circuit is increased; if the four wires in the box have resistances of 1, 2, 3 and 4 ohms, removal of all the plugs would give a resistance of 10 ohms.

A **rheochord** is a wire, *r r r*, and slider, *s s*, so disposed that a very low but variable resistance can be offered as a *deriving*, or 'shunt,' circuit, by the side of a *principal* circuit of higher resistance. It affords means of dividing a current into two parts, and of thus obtaining any desired small fraction of the current of a single Daniell cell, the larger part passing through the rheochord, *r*, *r*, *r*, which is of small resistance, the

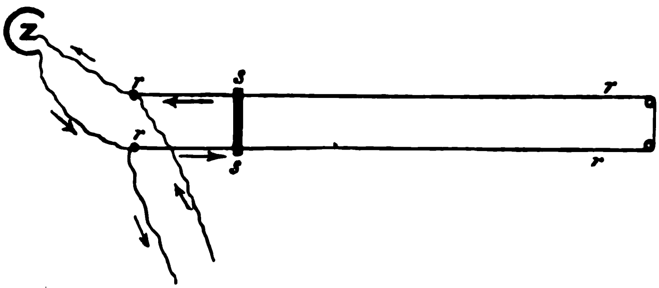


FIG. 114.—A SIMPLE RHEOCHORD.

A key (not shown in figure) is to be used between the battery and the rheochord, not between the rheochord and electrodes.

smaller part passing through the principal circuit, which is of high resistance, and includes the electrodes and the nerve or muscle. If, for instance, the current of a Daniell is made to branch (*a*) through a rheochord with a resistance of 1 ohm, (*b*) through a nerve with a resistance of 9,999 ohms, then the current in the shunting or rheochord circuit will be $\frac{9999}{10000}$, the current in the nerve circuit will be only $\frac{1}{10000}$ of the entire current of the Daniell cell. The rheochord as a deriving circuit is to the principal circuit what the galvanometer shunt is to a galvanometer; by means of a slider the resistance of the deriving circuit, and consequently the magnitude of the current diverted into the principal circuit, can be increased or diminished at will. One of the chief uses to which the rheochord is put is in rheotome observations, to compensate any current of injury which may accidentally be present in muscle or nerve.

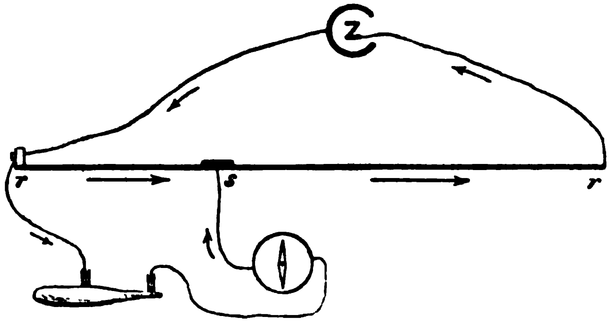


FIG. 115.—A STRAIGHT RHEOCHORD (MONOCHORD) AS DISPOSED FOR COMPENSATION.

Electrical Resistance is measured by means of a *Wheatstone bridge*, the principle of which is as follows. The current of a battery is sent through a branched circuit containing three known resistances, A, B, C, the unknown resistance, x, and a galvanometer placed in the bridging wire. Two of the resistances, A and B, are fixed; the third resistance, C, is variable, and used as the measuring resistance. When the relation $\frac{x}{C}$ is equal to $\frac{A}{B}$ there is no current through the galvanometer, which therefore acts as a balance indicating when C has been made too large or too small. The equality $\frac{x}{C} = \frac{A}{B}$ having been found

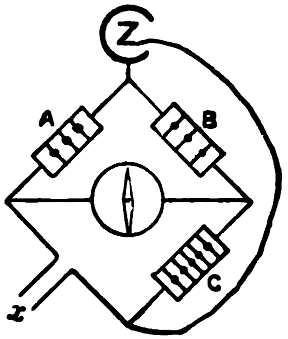


FIG. 116.—WHEATSTONE BRIDGE.

by adjustment of C, the value of the unknown resistance, x, is found by simple calculation from the known values A, B and C; thus $x = C \times \frac{A}{B}$ If A and B are taken of equal resistance, the value of x is equal to that of C, as found by trial. These facts should be realised by determinations of the resistance of muscle and of nerve as ordinarily arranged in physiological experiments. The following very approximate numbers will serve to give an idea of the resistances commonly dealt with in such experiments.

Resistance of du Bois-Reymond's unpolarisable electrodes .	10,000	ohms
" of d'Arsonval's silver electrodes	100,000	"
" of frog's gastrocnemius	10,000	"
" of 1 cm. frog's sciatic	100,000	"
" of human skin (according to moisture)	1,000 to 100,000	"

The transverse resistance of nerve is five times as great as its longitudinal resistance; the transverse resistance of muscle is 4 to 9 times as great as its longitudinal resistance (Hermann).

Current diffusion—Distribution of potential.—A current led through a bulky conductor, *e.g.* the human body, by two electrodes, *diffuses* throughout that conductor in accordance with Ohm's law. It is most concentrated—*i.e.* its density is greatest—along a line of least resistance

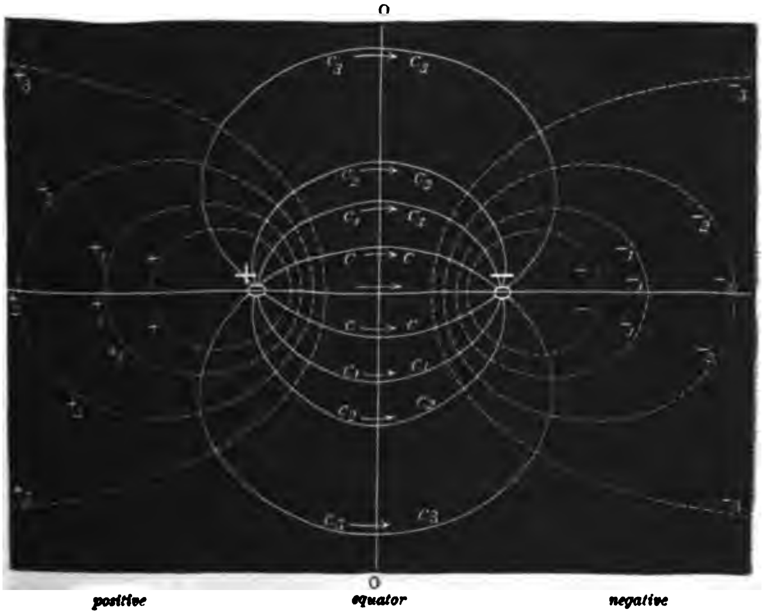


FIG. 117.

between the two electrodes; it is less and less concentrated along curved lines further and further removed from this current axis. The nature of current diffusion and of the corresponding distribution of potential will be best appreciated by the study of a simple case—a large vessel of salt solution into which the current of a Daniell cell is led by a fixed pair of silver chloride electrodes touching the surface, and from which current can be led off by a movable pair of electrodes to a galvanometer. It will be found by trial that most current passes in the straight line + —, less and less current along c_1, c_2, c_3, &c.; that if both leading-off electrodes are on points of the line O O, or on any two points of the lines $+_1$, $+_1$, $+_1$, or, $+_2$, $+_2$, $+_2$, &c., no current passes; that a greater current is obtained if the leading-off electrodes are on opposite sides of the line O O than if they are on the same side. Using the leading-off electrodes in connection with an electrometer instead of a galvanometer, we shall be able to test the electrical pressure differences between various points of the surface, and shall find that all that surface on the + side of O O is positive to all that surface on the — side of O O; that the greatest difference is at and near the two points + and —; that there is no difference between any two points on O O, or on any curved line, $+_1$, $+_1$, $+_1$, $-_1$, $-_1$, $-_1$, &c. By these experiments we shall have defined the line + — as the *current axis*; c_1, c_2, c_3, as *lines of current diffusion*; O O, cutting the middle of + — at right angles, as the *equator*

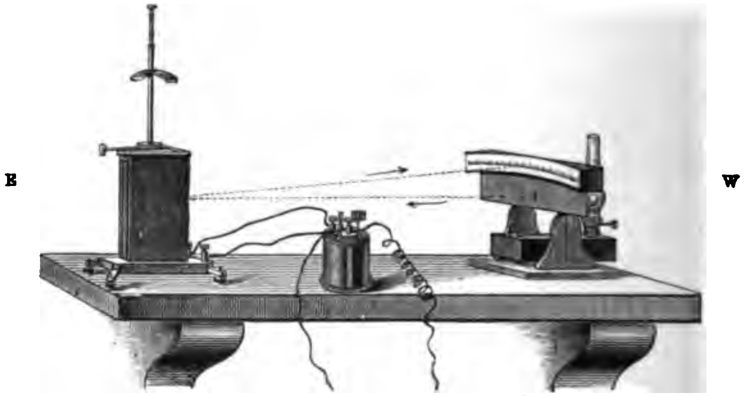


FIG. 118.—SIDE VIEW OF GALVANOMETER AND SHUNT, LAMP AND SCALE.

The galvanometer and scale are placed east and west, and appear as if viewed by an observer standing on the north side; the path of light is indicated by dotted lines. The essential parts concealed by the galvanometer case are diagrammatically given in fig. 119.

or line of zero pressure, dividing an area of *positive* potential from an area of *negative* potential; $+_1$, $+_1$, $+_1$, $-_1$, $-_1$, $-_1$, &c., as *equi-potential lines*, *i.e.* as lines all points of which are at the same electrical level.

We shall find a very simple illustration of these elementary principles when we come to the study of the electrical variations of the human heart (p. 388).

The Galvanometer (Thompson's).—The direction and magnitude of a current is ascertained by the galvanometer. For clinical purposes it is sufficient to use a small instrument graduated from one to twenty milliampères; for laboratory purposes, *e.g.* for nerve-currents, an instrument at least 10,000,000 times more sensitive is required, owing to the magnitude of the resistances and the smallness of the differences of potential to be dealt with. A galvanometer of this kind is of *high resistance* (5,000 to 20,000 ohms). When necessary its sensitiveness is reduced by the use of a *shunt*, which carries off $\frac{9}{10}$ or $\frac{99}{100}$ or $\frac{999}{1000}$ of a current through a deriving circuit, $\frac{1}{9}$ or $\frac{1}{99}$ or $\frac{1}{999}$ of the resistance of the galvanometer, and therefore leaving to pass through the galvanometer $\frac{1}{10}$ or $\frac{1}{100}$ or $\frac{1}{1000}$ of the original current. For *thermo-electric* measurements, in which small differences of potential through a very small resistance are dealt with, a galvanometer of *low resistance* (less than 1 ohm) is employed. The principle upon which both these galvanometers depend is, that a suspended magnet surrounded by coils of wire is deflected when a current passes through the wire, the direction of the deflection and its amount indicating the direction and amount of the current. The suspended magnet (or system of magnets) is made very nearly 'astatic,' *i.e.* not to set too strongly towards the magnetic pole, and can be made more or less astatic, and therefore more or less sensitive, by means of a separate magnet which can be adjusted to neutralise the 'set' of the suspended magnet more or less completely, or if necessary be reversed so as to increase it. The movements of the suspended magnet are shown greatly magnified by means of a light mirror which reflects a beam of light on to a horizontal scale. If desired, the varying positions of the spot can be photographed upon a travelling sensitive surface placed behind a slit in the scale (*e.g.* fig. 168).

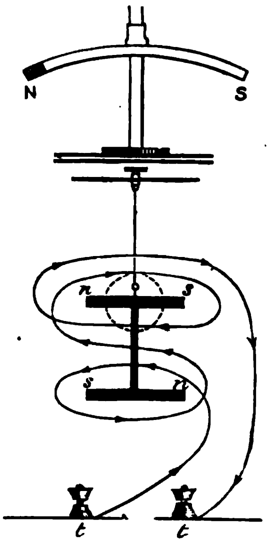


FIG. 119.

Astatic couple of magnets *n s*, *s n*, suspended by a silk fibre and carrying a mirror (indicated by the dotted circle); the surrounding line and arrows indicate the disposition of the coils; N S is the neutralising or controlling magnet. All these parts are represented as if viewed by an observer standing west, *i.e.* in the position of the lamp in fig. 118.

In Wiedemann's galvanometer the adjustments are effected by movable coils, fine wire coils being used for currents through high resistance, coarse wire coils for currents through low resistance; the coils can be set nearer or further from the suspended magnet, the deflections of which are read through a telescope.

In d'Arsonval's galvanometer the coil is suspended between two strong magnets, and is itself deflected by the currents under observation. The deflections are observed by a telescope, or (with sufficiently strong currents from one milliampère upwards) can be recorded by means of a light pen fixed to the coil on a smoked cylinder moving round a horizontal axis. Such records are particularly desirable in experiments on the excitability of human muscle and nerve.

The galvanometer is an indicator of current, but by adopting the method of **compensation**, it becomes an indicator of potential, being in this case used as a balance to show the equality of two opposite potentials—the galvanometer circuit being then free of current. The simplest way of measuring the potential difference[1] at any two points of muscle or nerve &c. is as follows (fig. 120): A Daniell cell is connected with the two ends of a rheostat, divided into two parts, one of lower resistance, r, the other of higher resistance, R. With the high external resistance, the P.D. at the two terminals is equal to the full E.M.F. of the cell (*i.e.* 1 Dan. or about 1·1 volt), or differs from it by a negligible fraction (*i.e.* $\frac{\text{internal resistance}}{\text{external resistance}}$), and the P.D. at any two points of the circuit is proportional to the resistance between these points. Thus the P.D. at two points of a muscle is ascertained by finding the resistance, r, at which it is balanced (*i.e.* no current through the galvanometer); it is then equal to $\frac{r}{r+\text{R}}$. For example, if the balance is obtained with $r = 250$ ohms, and $r + \text{R} = 7500$ ohms, the muscle potential is $\frac{250}{7500}$, or ·033 Dan. The principle is precisely the same as that of the rheochord, but the total resistance in the battery circuit is much greater.

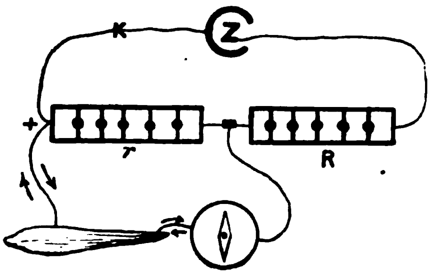


FIG. 120.—MEASUREMENT OF POTENTIAL BY COMPENSATION.

An indispensable condition to be observed whenever the electrical excitability of exposed nerve or muscle is to be exactly studied, and still more whenever currents from living tissues are to be led off to a galvanometer, is the employment of **unpolarisable electrodes** (du Bois-Reymond). Their construction is as follows:—A carefully amalgamated zinc rod dips into a saturated solution of zinc sulphate, which in turn communicates with a plug of china clay made up into a paste with normal saline; a glass tube shaped according to requirements, and fixed in a suitable holder, contains the several constituents of such an electrode, which has the following qualities: it is unpolarisable by weak currents; it is not itself a source of electromotive force; it is of high resistance; it can be applied to living tissues without appreciably injuring them. A pair of unpolarisable electrodes should be tested before use by bringing their plugs into contact while they are connected with the galvanometer; they should then give little or no current. A more convenient (though less perfect) unpolarisable electrode is that of d'Arsonval; it consists of a silver rod coated with fused silver chloride dipping into a tube filled with normal saline.

---

[1] 'Potential difference,' 'electromotive force,' are shortly expressed by the initial letters P.D., E.M.F.

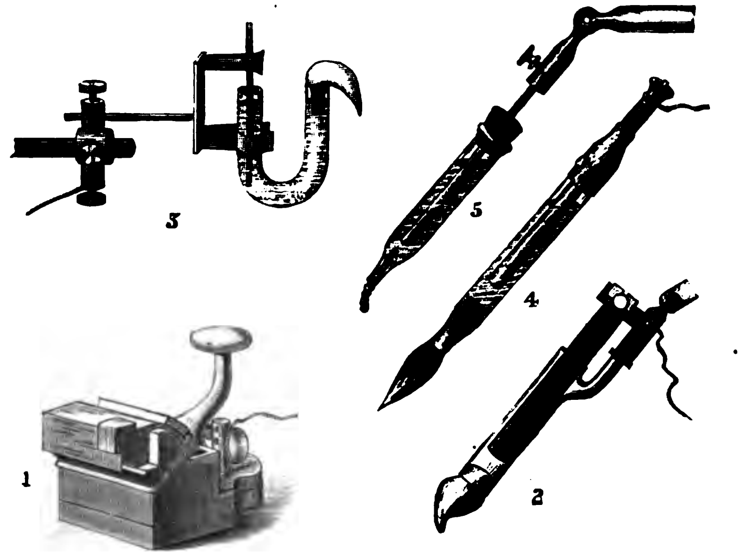


Fig. 121.—Several Models of Unpolarisable Electrodes.

1 and 2, du Bois-Reymond's; 3, Burdon-Sanderson's; 4, von Fleischl's; 5, d'Arsonval's.

In 1, 2, 3 and 4 the component parts are zinc, zinc sulphate and saline clay; in 5 a silver rod coated with fused silver chloride dipping in normal saline contained in the tube from which a thread projects.

The Rheotome (Bernstein, Hermann) is an instrument by which a series of stimuli can be led into muscle or nerve, and the consequent series of excitatory effects led off to a galvanometer, during definite periods at regular intervals after stimulation. This is in principle effected by a revolving bar carrying two contacts, one in the primary or exciting circuit, 1 1 1, one in the galvanometer or electrode circuit, 2 2 2 (the latter being in the form of a metal horse-shoe ending by two brushes of fine wires which rub against the metal plates connected with the galvanometer and leading-off electrodes). If the bar revolves once a second, and completes the galvanometer circuit by a pair of metal pieces occupying $\frac{1}{100}$ part of the circle, the circuit is closed at each second for $\frac{1}{100}$ sec. The circle carrying the primary contact is movable round the circle carrying the galvanometer contact; it can be set so that the two contacts are made simultaneously, or so that the galvanometer contact, lasting $\frac{1}{100}$ sec., is made $\frac{1}{100}$, $\frac{2}{100}$, $\frac{3}{100}$, &c. sec. later than the primary contact. We can thus obtain a repetition of effects, and 'tap the excited muscle or nerve at each revolution—*i.e.* each second—for a period of $\frac{1}{100}$ sec. immediately after each stimulus, or $\frac{1}{100}$, $\frac{2}{100}$, $\frac{3}{100}$ sec. later. Combinations suitable for various purposes are obtained by varying the rate of revolution, the length of the galvanometer contact, and its angular distance from the exciting contact; *e.g.* if the bar revolves 10 times a second and makes contact for $\frac{1}{20}$ part of the circle, the circuit is closed for $\frac{1}{200}$ sec.; if for $\frac{1}{50}$ part of the circle, the circuit is closed for $\frac{1}{500}$ sec. Any injury or other current from the tissue must be kept exactly compensated during experiment.

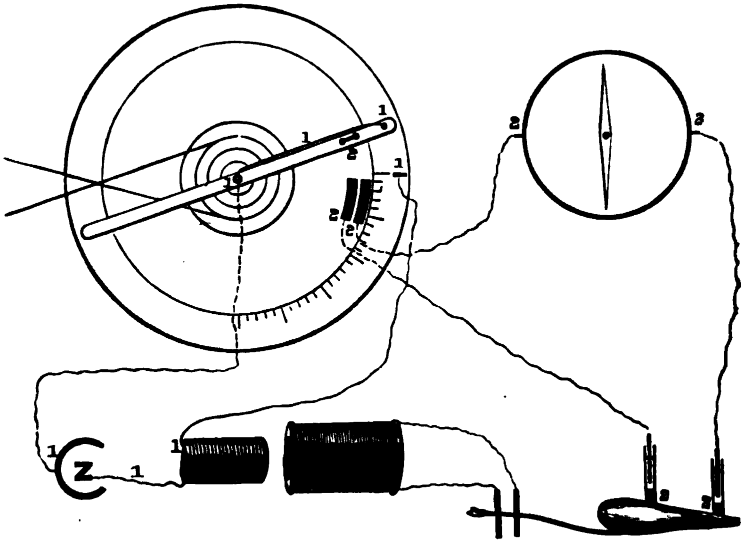


FIG. 122.—SCHEMA OF A RHEOTOME.

1 1 1 1 is the primary or excitation circuit; 2 2 2 2 is the galvanometer circuit. Any current from the quiescent muscle would be balanced by a compensator, as shown in fig. 115.

Thermo-electric measurements.—A thermo-electric couple is the surface of junction of two different metals which form a completed circuit. If the junction is heated an electrical current passes across the junction and around the circuit, as is seen by the deflection of a galvanometer placed in the circuit. Different pairs of metals act more or less strongly when equally heated. The couples usually employed are bismuth—antimony; or german silver—iron; the arrows indicating the direction of the current through the heated junction. Within certain limits, strength of current is in direct proportion with temperature of junction; it is thus possible to read temperature by means of the galvanometer (which indicates strength of current).

If two similar couples are in circuit with a galvanometer (as shown in the second diagram), and both junctions are heated equally, no current passes through the galvanometer, the current through one couple from B to A being balanced by the opposed current through the other couple from B to A. But if there be any inequality of temperature between the two couples, then a current passes, the direction of the deflection indicating which is the warmer couple. We may thus readily determine differences of temperature by plunging thermo-electric couples in the shape of needles into the tissues. Or, having plunged two needles symmetrically into a frog's gastrocnemius of each limb, we may excite first one, then the other sciatic nerve and observe deflections first in one, then in the opposite direction, indicating the production of heat in the muscular contraction first on one,

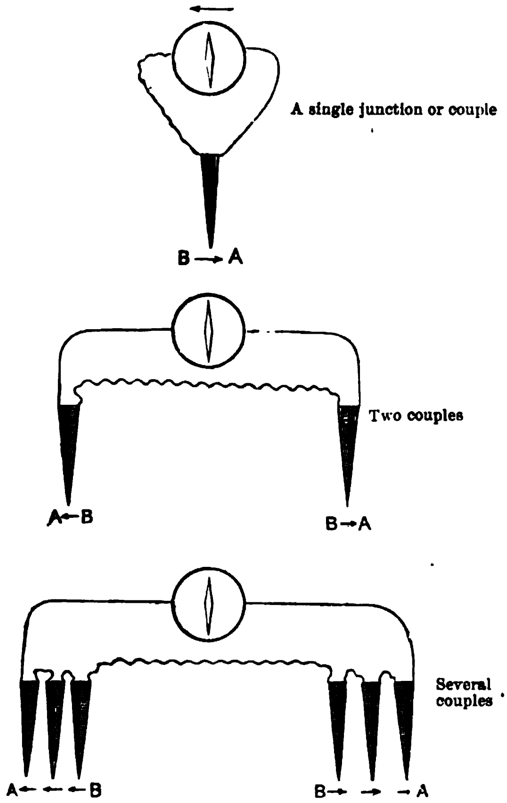


FIG. 123.—SCHEMA OF THERMO-ELECTRIC COUPLES.

then on the opposite side. For very delicate observations two series of couples are used as thermopiles.

Lippmann's Capillary Electrometer.—A glass tube drawn out at one end to a fine bore (20 to 30 μ) is filled with mercury and connected with an apparatus by means of which the pressure can be raised or lowered. The capillary end of the tube dips into ten per cent. sulphuric acid. Two platinum wires fused through the glass establish connection with the mercury and with the sulphuric acid respectively. By means of the pressure apparatus mercury is forced into the capillary and adjusted until it takes up a position of rest in the field of a microscope. The pressure of the mercury and the capillarity of the tube are in equilibrium; the lower surface of the mercury is in a state of tension, which is very easily increased or diminished by variations

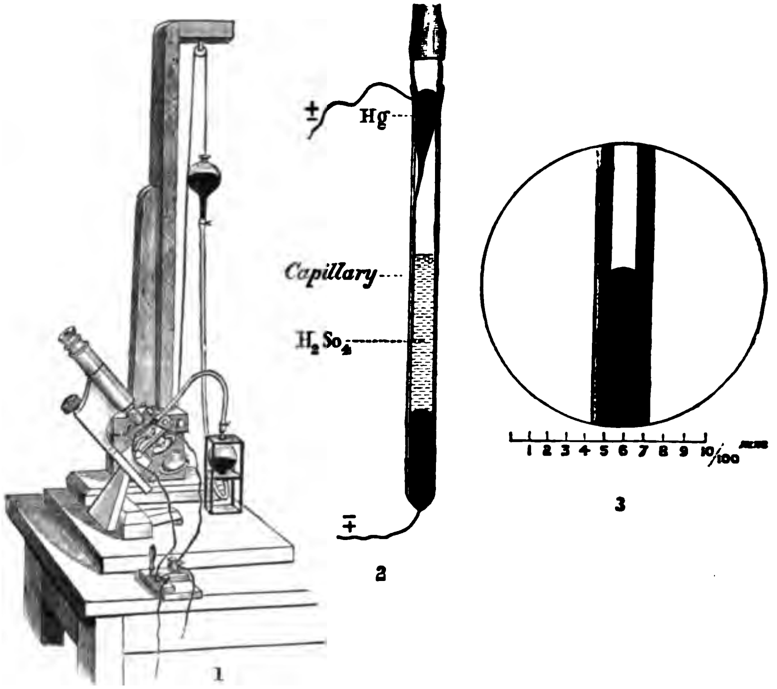


FIG. 124.—LIPPMANN'S CAPILLARY ELECTROMETER.

1. Pressure apparatus and microscope on the stand of which the capillary tube is fixed.

2. Capillary tube dipping into H_2SO_4 in a surrounding tube, and in connection with pressure apparatus (the mercury in the lower part of the surrounding tube serves only to establish connection with the platinum wire).

3. The capillary tube and column of mercury as seen in the field of the microscope. (Scale in $\frac{1}{100}$ths mm.)

of electrical potential. The instrument is in fact an exceedingly delicate electrical manometer; a rise of electrical pressure on the mercury side or a fall of electrical pressure on the sulphuric acid side, causes the mercury to move towards the point of the capillary; a fall of electrical pressure on the mercury side or a rise on the sulphuric acid side causes the mercury to recede from the point of the capillary. The instrument accordingly is an indicator of 'potential' or 'pressure,' not of 'current.' Its delicacy is such that it will react to as little as $\frac{1}{40000}$ volt. It offers, moreover, the following advantages:—the indications are practically instantaneous, free of lost time, and of after-

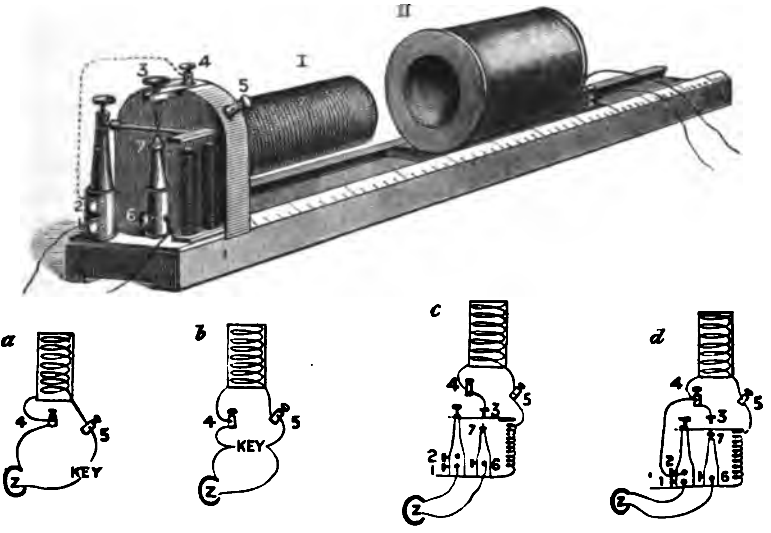


Fig. 125.—Du Bois-Reymond's Induction Apparatus.

The numbers 1 to 7 indicate the terminals and contact screws connected with the primary coil.

For single shocks the two battery wires are to be connected with the terminals 4 and 5, which are at the two ends of the primary wire.

(*a*) *Unmodified shocks* are obtained when a key is used to interrupt one of the wires.

(*b*) *Reduced shocks* are obtained when a key is used short-circuiting the primary wire.

(*c*) *For repeated shocks* (*ordinary*) the two battery wires are to be inserted at 1 and 6. The circuit now includes the spring interrupter and the wire of the electro-magnet by which the circuit is made and broken at the contact screw 3; the contact screw 7 is kept out of use by being lowered.

(*d*) *For repeated shocks* (*modified*) the battery wires are left, as before, at 1 and 6. A short thick side wire is placed between 2 and 4. The contact screw 3 is raised out of range of the spring, and the contact screw 7 is raised until it comes within range of the spring.

The electrode wires are in each case connected with two terminals (not seen in figure) forming the two ends of the secondary wire.

oscillation; the resistance in circuit is immaterial; unpolarisable electrodes may for most purposes be dispensed with.

The **induction apparatus** of du Bois-Reymond is the electrical instrument in most common use in the laboratory, as well as in ordinary clinical study. It consists of a cell which supplies electromotive force, a primary or thick wire coil, and a secondary or thin wire coil. Various kinds of interrupters or keys are placed in the primary circuit (*i.e.* between the battery and primary coil), and the electrodes used for excitation are at the two ends of the secondary circuit.

The principle upon which the working of the apparatus depends is as follows:—When a current flows through a wire it induces an opposite current in a neighbouring wire. When by closing a key, current is sent through the primary coil, the current in each turn of the wire induces an opposite current in neighbouring turns (make extra-current); when by opening a key, current through the primary coil is suddenly broken, the cessation of current in each turn of wire induces a similar current in every other turn (break extra-current). The direction of the make extra-current is opposite to that of the original current; that of the break extra-current is in the same direction; hence the former is much less sudden and a less effectual stimulus than the latter, as may be appreciated by placing on the tongue two wires connected with a coil and cell, and a key to make and break the current through the coil and tongue.

In the ordinary use of the coil the currents of the primary circuit *induce* other currents in the secondary circuit, these being spoken of as the make- and break-currents. Of these two currents the break is by far the sharper; both currents are stronger or weaker according as the secondary is nearer to or farther from the primary coil; both these points should be appreciated by applying electrodes of the secondary coil to the tongue. For most experiments on nerve and muscle it is necessary to reduce the disparity between make and break, and this is usually done by means of the *Helmholtz side wire*, which acts as a shunt to the primary coil. In the coil thus modified the primary circuit is never completely interrupted; a weakened make-current passes the coil when the side circuit is broken, and a weakened break-current is produced when the side circuit is completed.

Rapidly repeated shocks (*faradisation*) are usually obtained by means of an automatic interrupter in the primary circuit; this is composed of an electro-magnet the wire of which is continuous with the wire of the primary coil, an iron armature, and a spring contact, also in the primary circuit; the battery wires are connected to the terminals 1 and 6. The play of the interrupter is as follows:—Make of the current draws down the armature and breaks the current at the spring contact 3 ; break of the current lets go the armature and current is again made by the spring contact. This see-saw action is repeated forty or fifty times per second, and is the cause of the noise characteristic of induction coils.

Electrical Chronographs.—Measurements of time are in constant requisition for physiological purposes, and among the various means adopted, an electrical method is the commonest, as we can thus most easily take a chronographic record simultaneously with the movement recorded. The component parts of electrical time-markers are a small electro-magnet with a recording lever attached to the armature, and with its coil in the circuit of a cell and interrupter. The interrupter may be a tuning-fork or a reed of given vibration-frequency, with a platinum point, which by means of a second electro-magnet is kept vibrating to and from a clean surface of mercury, making and breaking circuit, attracting and releasing the chronograph armature, and thus marking time in corresponding fractions of a second. The time-markers in ordinary use are those of Despretz and of Pfeil. If the apparatus is used as a signal, the electro-magnetic interrupter is replaced by a key, and the lost 'time' of the signal itself should be determined ; this is usually from ·0005 to ·0010 second.

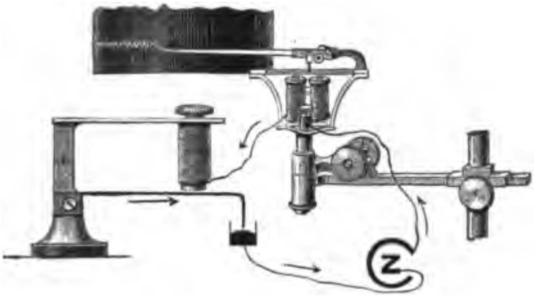


FIG. 126.—CHRONOGRAPH, OR TIME-MARKER.

Composed of battery, vibrating reed (Page's), signal (Pfeil's).

MUSCLE.

The muscles of animals, anatomically as well as physiologically considered, are divisible into two separate and distinct systems—(1) those which form the chief bulk of the walls of the hollow viscera and of the blood-vessels; (2) those which are attached to the bones. Muscles of the first kind are not subject to the will, and are therefore characterised as *involuntary*; they are composed of long nucleated cells which are not striped; hence such muscle is characterised as *smooth* or *non-striated.* Muscles of the second kind are under the control of the will, and are therefore called *voluntary*; they are composed of fibres which are transversely striped; hence such muscle is also characterised as *striated.* Between these two typical kinds—the smooth involuntary and the striated voluntary—a third kind must be reckoned, viz. cardiac muscle, which is intermediate in its anatomical and physiological characters. Voluntary striated muscle is further distinguishable in many animals into two varieties, viz. *pale* and *red.* The pale variety is the more highly organised; it exhibits more marked striation and less abundant nuclei than the red variety.

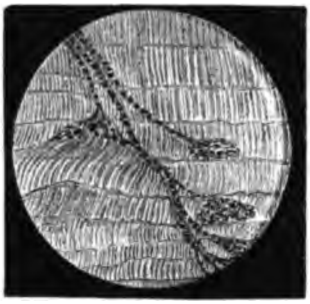
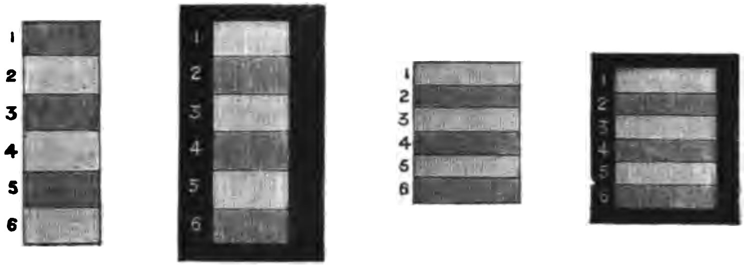


FIG. 127.—MOTOR NERVE-ENDINGS IN SNAKE'S MUSCLE.

Involuntary muscle is chiefly supplied by non-medullated nerve-fibres, but also receives a smaller proportion of medullated fibres. The actual termination of nerve fibre in involuntary muscle is not known with certainty; abundant networks of fibres are to be seen, and in connection with them ganglionic cells. Voluntary muscle is chiefly supplied by medullated nerve-fibres, which form definite structures at their junction with the muscular fibres, the most characteristic of these being motor end-plates.

Histological characters of resting, of contracting, and of rigid muscle.—The ultimate structure of a striped muscle fibre has been for long a vexed question. Upon one important point all observers are agreed, viz. that the sarcolemma, or sheath of the fibre, contains contractile solid particles (sarcous elements or sarcostyles) and a fluid non-contractile portion. That the fibre is not transversely divided by a series of partitions (Krause's membrane) is considered to be proved by Kühne's observation of a nematode worm moving freely in a living muscle fibre without meeting with any apparent resistance until coagulation had occurred. By microscopic observation of a tetanised muscle fibre, or of a muscle fibre fixed in a state of partial contraction by osmic acid, it has been found that the shortening and thickening of the fibre are attended with an obvious approximation of its transverse striæ, and with a by no means obvious reversal of the optical relations of the striæ, the dark broad band of the resting muscle becoming the light narrow band of the contracting muscle. Viewed by polarized light, there is no such transposition; the dark band of an uncontracted fibre and the light band of a contracted fibre are both doubly refracting (anisotropous) and appear as light bands in a dark field. We must, however, make the express reservation that these observations refer in both cases to dead muscle, and that it is nowise certain that the partially contracted parts of muscles fixed by osmic acid give the true picture of a natural contraction. And as a matter of fact it is only dead muscle which exhibits under polarized light the regular and well-marked alternation of doubly refracting light band and singly refracting dark band: in living muscle almost the whole of the substance is doubly refracting; singly refractile substance in the form of lines and dots is relatively



A. Fibre at rest; ordinary light. B. Fibre at rest; polarised light. C. Contracted fibre; ordinary light. D. Contracted fibre; polarised light.

FIG. 128.

The accompanying very diagrammatic figure is intended only as a guide to the description given above, and not in any degree to imitate the actual appearances. The odd numbers 1, 3, 5 point to contractile substance, dark in A, light in C; light in B and D (*i.e.* doubly refracting or anisotropous). The even numbers 2, 4, 6 point to non-contractile fluid, light in A, dark in C; dark in B and D (*i.e.* singly refracting, or isotropous).

scanty; and, as may readily be believed, these optical properties have not been observed to alter during the act of contraction.

Chemical composition of muscle: its alteration by activity and in rigor.—Muscle—or, to call it by its popular names, flesh or meat—is mainly composed of water and of proteid; the elementary composition of dry flesh is thus closely similar to that of dry proteid or of dry blood (v. p. 9). Besides its proteid constituents, muscle contains a comparatively small quantity of other nitrogenous bodies, of inorganic salts, and of carbohydrates; a variable amount of fat is usually associated with muscle, but is not, properly speaking, a constituent of pure muscle. The average composition of muscle is as follows:—

Water	77·5
Proteid	20
Other nitrogenous bodies (creatin, xanthin)	1
Salts (phosph. and K.)	1
Carbohydrates (glycogen, inosit, lactic acid, sugar)	·5

The red colour of muscle is partly due to blood-pigment, partly to a special pigment—myohæmatin (MacMunn); ferments are also present—viz. the myosin ferment and a peptic ferment.

We have to study (1) the chemical differences between living and dead muscle; (2) the chemical differences in dead muscle, which before death was at rest or in forced activity.

The consistence of a living irritable muscle differs from that of dead muscle which has entered into 'rigor mortis'—the former is soft and elastic, the latter is firm and very imperfectly elastic—'doughy.' The difference depends upon the fact that living muscle consists of separate solid and liquid parts—the sarcous elements and muscle plasma—while in dead muscle the liquid part (plasma) has undergone coagulation and has yielded myosin. The rigor or coagulation of muscle is indeed closely analogous with the coagulation of blood: it depends upon the conversion of a body present in muscle plasma (myosinogen) into myosin just as the coagulation of blood depends upon the conversion of a body present in blood plasma (fibrinogen) into fibrin, and it is probable that in the case of muscle as in that of blood the conversion is effected by the agency of a ferment (Halliburton). The myosin coagulum exhibits the following remarkable difference from the fibrin coagulum: both are soluble in 10 per cent. solution of sodium chloride, the first-named body the more readily; the dissolved myosin yields a renewed coagulum when its salt solution is diluted; not so the dissolved fibrin (Halliburton). The myosin coagulum having formed is thus easily unmade and remade out of the body; *perhaps* this is also the case in the body.

Preparation of muscle-plasma.—The coagulation of muscle-plasma is delayed by cold. The fresh irritable muscles, preferably of frogs, are accordingly frozen, minced, pounded, and pressed, all instruments used being cooled; a syrupy alkaline liquid is expressed, which is coagulable at ordinary temperatures or on dilution with cold distilled water. This liquid is *muscle-plasma*, and the body which separates from it when coagulation occurs is *myosin.* The fluid which remains after removal of the coagulum is *muscle-serum*, and it is remarkable that the coagulation is accompanied with the formation of acid. Alkaline muscle-plasma yields acid muscle-serum.

Muscle-serum contains in solution at least three proteids—(1) muscle-globulin, coagulated at a temperature of 63°; (2) muscle-albumin coagulated at 73°; (3) muscle-albumose uncoagulated by heat but precipitated by nitric acid in the cold. The three bodies are separable as follows: the globulin is separated by saturation with $MgSO_4$, the albumin is separated by heat coagulation, the albumose remains in the filtrate.

Preparation of myosin.—If muscle-plasma is allowed to fall drop by drop into distilled water, myosin coagulates at once, and is obtained in the form of little balls. Myosin may also be obtained from rigid muscle in which it has already formed, by pounding with sodium chloride, then adding water to make a ten per cent. solution of the amount of salt used; myosin is soluble in this, and is precipitated by pouring the solution thus obtained into a considerable quantity of water, or by dialysis. Myosin belongs to the class of globulins, and is as such insoluble in distilled water, soluble in solutions of neutral salts ($NaCl$, $MgSO_4$, Na_2SO_4); in solution it coagulates when heated to between 55° and 60°.

Sarcolactic acid.—Living resting muscle has a neutral or alkaline reaction; dead rigid muscle has an acid reaction. The difference is due to *sarcolactic acid* produced during rigor, *i.e.* accompanying though not necessarily caused by the conversion of myosinogen into myosin. We have already seen that the rigor of muscle is accompanied with a production of carbon dioxide (pp. 131–33); we are about to learn that the same two changes also accompany the normal activity of muscle. But whereas in rigor the acidification is the more prominent phenomenon, in normal action the chief event is the production of CO_2; these considerations suggest as probable that the lactic acid ($C_3H_6O_3$) produced in muscular katabolism is a stage towards the production of CO_2; in full action muscle may produce lactic acid, and then decompose it further into CO_2; in declining action muscle may produce lactic acid and fail to complete the process.

Inosit, or muscle-sugar ($C_6H_{12}O_6,2H_2O$), is a minute and variable constituent of muscle. Unlike grape sugar, it has neither rotating action on polarised light, nor reducing action upon Fehling's solution; it is a crystalline body and can undergo lactic but not alcoholic fermentation.

Rigor mortis as manifested by the human body is of medico-legal interest, as yielding some indication of the time at which death may be presumed to have occurred. From observations on tetanised muscles and on hunted animals we learn that previous muscular activity hastens the advent of rigor; from observations on man—deaths by accident, or in hospitals, or in battle—we learn that the 'death-stiffening' begins earliest in a person surprised in active exertion at the time of death; on worn-out bed-ridden patients it begins early, is ill-developed, and soon passes off. It usually begins two or three hours after death and lasts for two or three days, but soldiers have been found in attitudes indicative of its immediate onset, and it sometimes does not commence before several hours after death. The order of its manifestation on the human subject is from above downwards, in the jaw, neck, arms, and legs. After a period varying from a few hours to a few days, rigor passes off and in a reverse order, by resolution of the coagulated myosin, and now putrefaction sets in.

Differences between active and resting muscle.—There are only two known chemical differences between living resting and living active muscle, viz. the reaction and the amount of CO_2—living resting muscle is neutral or faintly alkaline in reaction, living active muscle is slightly acid, the acidity, like that of rigor, being due to sarcolactic acid. In its chemical effects, activity is thus comparable with partial death, and we may add to the comparison by the observation that whereas death is attended by the complete and final coagulation of myosin, prolonged activity is marked by an incompleteness of relaxation, which *may* be—though it cannot be *proved* to be—due to a temporary coagulation of myosin. The similarity of the electrical change, which accompanies the excited and the dying states, and the evolution of heat which accompanies contraction and rigor, may be alluded to as further points of resemblance. Fick offers as the most probable hypothesis to account for the phases of contraction and relaxation (1) a production of lactic acid and of myosin during the former, (2) a production of CO_2 and a resolution of myosin during the latter. In pursuing our examination beyond this stage, it is to be remembered that the chemical differences between active and inactive muscle relate in each case to muscle which is dead, having necessarily been killed in the process of analysis. In correspondence with the statement just made, that muscular activity is attended with an evolution of CO_2, it is found that the CO_2 collected by means of the gas-pump (*a*) from rigid previously active muscle, (*b*) from rigid previously resting muscle, is of greater amount in the second case than in the first; *i.e.* previously active muscle contains less CO_2 yielding substance than previously resting muscle. Further than this only some isolated statements have been made by various observers to the following effect:—

1. Previously active muscle yields a smaller amount of water-extractives but a larger amount of alcohol-extractives than previously resting muscle (Helmholtz).

2. Pyrogallic acid is more readily oxidised by an aqueous extract of resting muscle than of tetanised muscle. Sulphate of indigo is more readily reduced by an aqueous extract of tetanised muscle than of resting muscle (Grützner).

3. Resting muscle contains more glycogen; tetanised muscle contains more sugar (Nasse).

The Properties of Muscle.—The physiology of muscle is almost entirely derived from the study of voluntary muscle, and the considerations upon which we are now entering relate almost exclusively to voluntary muscle.

Living muscle possesses two chief properties: (1) It is extensible and elastic; (2) it is excitable and contractile.

Extensibility and Elasticity; Viscosity.—Muscle can be stretched beyond its normal length, and can recover its original length when the extending force is removed, unless the extension has been excessive. Extensibility is demonstrated by the elongation of a muscle fixed at one end and weighted at the other; elasticity is demonstrated by the shortening when the weight is removed.[1] The magnitude of these alterations is conveniently studied by means of a long light lever, which is attached to the lower end of the muscle, and records the changes of length upon a smoked surface. A frog's gastrocnemius so disposed, and extended successively by weights of 10, 20, 30, 40, &c. grammes, will show for each successive equal increment of 10 grammes a diminishing increase of length; *i.e.* the elongation increases with the increased weight but in a diminishing ratio; for instance, the elongation when the weight is increased from 20 to 30 is less than when the weight was increased from 10 to 20; it is less still when the weight is increased from 30 to 40 and so on. In this respect the extensibility of muscle resembles that of arteries, and differs from that of inorganic substances, *e.g.* caoutchouc or indiarubber, which give a series of elongations nearly proportional to the weights used. The recovery of length dependent on elasticity is observed in either case by the successive removal of the weights. It will be noticed in the case of muscle that each recovery of length as each weight is removed is greater than the preceding one, and that the recovery is not quite perfect. It is,

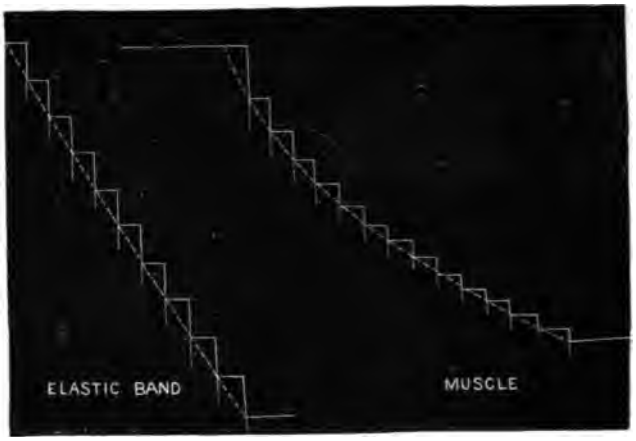


Fig. 139.

---

[1] Considerable confusion still prevails in the use of the term 'elasticity.' Sometimes it is improperly used to denote the 'yieldingness' of a body, which after it has been stretched beyond its length returns to its original length. This use of the term is incorrect, extensibility is the correct word to use. Sometimes it is used to denote resistance to stretching, but this is inconvenient, for in this sense of the term an inextensible body has great elasticity. It is preferable to limit the term to express the force with which a stretched or compressed body tends to *return* to its original dimension.

however, usual, and no doubt correct, to say that the elasticity of muscle in its normal relations is perfect; though, out of the body and abnormally stretched, the muscle does not exhibit this perfect elasticity. Active muscle is more extensible than resting muscle; rigid muscle is less extensible than normal muscle, and its elasticity is very imperfect.

If a muscle be weighted and left so, it will be noticed that the weight causes an immediate elongation followed by a gradual elongation which continues in a diminishing degree for an indefinite time. If a weighted muscle be relieved of weight, it will be noticed that an immediate elastic shortening is followed by a gradual indefinite shortening. These after-effects (viscosity) are not characteristic of muscle, but common to all extensible and elastic substances; they are best demonstrated by causing the recording lever to mark its excursion upon a slowly travelling surface, *e.g.* a smoked cylinder fixed to the hour axis of an ordinary clock.

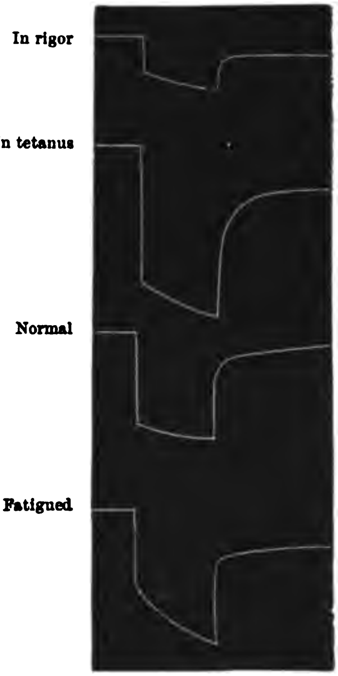


FIG. 130.—EXTENSIBILITY OF MUSCLE IN VARIOUS STATES.

Tested by 50 grammes applied for short periods.

Muscular extensibility and elasticity are useful in modifying sudden muscular contractions in the living body, rendering the application of their force more gradual, and thus obviating sudden jerks or rupture of tissue; moreover, the muscles are normally slightly stretched between their points of attachment to the bones, and are thus favourably disposed for prompt commencement and smooth execution of movements.

Contractility.—In common with all living tissues muscle possesses excitability, which property manifests itself as shortening or contraction; we say therefore that living muscle is *contractile*, *i.e.* able to contract, and that its characteristic vital property is '*contractility*,' *i.e.* ability to contract. Any agent which excites a muscle to contract is called a '*stimulus*;' it may be mechanical, thermic, chemical, electrical, or physiological. Of these various kinds of stimuli that which is usually employed experimentally is the electrical stimulus, and the electrical stimuli generally used are (1) the constant current and (2) induced currents. Normal muscular movement in the body is excited by the physiological stimulus which arises in the brain and is conveyed by motor nerves to muscle. Mechanical, thermic, and chemical stimuli are but little employed to stimulate muscle directly. The application of an experimental stimulus directly to muscle constitutes *direct* stimulation; the application of a stimulus to its motor nerve constitutes *indirect* stimulation, these expressions being used with especial reference to '*nerve-muscle preparations*,' which are usually composed of a sciatic nerve in connection with a gastrocnemius muscle removed from a recently killed frog.

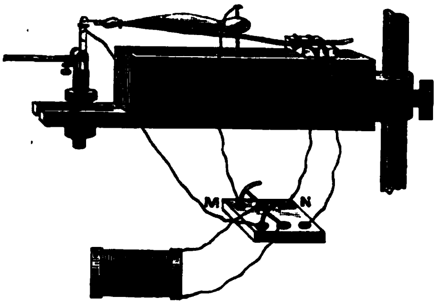


FIG. 131.

Sketch to show a myograph (the lever is cut off) and commutator without cross-wires arranged for direct and indirect excitation. Wires from secondary coil to middle pools of commutator; fine wires from left hand pair of pools to tendon of muscle and to pin through femur (circuit M) and from right hand pair of pools to a pair of electrodes across which the nerve is laid (circuit N); moving the cradle to left or right connects the secondary coil with muscle or with nerve, and current is sent through either by opening and shutting a key in the primary circuit (not shown in fig.)

Constant Current.—Stimulation with the constant current is effected when the current of a battery begins to pass and when it ceases to pass through a muscle, *i.e.* when it is *made*, and when it is *broken*, by closing and opening a key in the circuit of which the nerve or a muscle forms part. The muscle will contract each time the key is closed (make or closure contraction) or opened (break or opening contraction); it will remain quiescent while the current passes, *i.e.* while the key is left closed.

This is the rule, to which, however, there are exceptions; what is known as '*Wundt's tetanus*' is an enduring contraction which is apt to occur in a frog's muscle which is injured or traversed by a strong current; and on human muscle the effect termed '*galvano-tonus*'—which occurs on normal muscle during the passage of a strong current, on degenerating muscle during that of a comparatively weak current—is of a similar character.

If the stimulus is applied at one end of a muscle, the proximal portion begins to contract a little earlier than the distal portion, *i.e.* the contraction spreads as a wave from the point of excitations; its rate of propagation (in frog's muscle) being between 1 and 3 meters per second (Aeby).

Comparing the effects at make and break of the constant current, it will be found that the contraction at make is stronger than the contraction at break; to determine this relation it is necessary to graduate the strength of current and consequent strength of stimulation by means of the rheochord (p. 305). It will be found by further experiments that *the make contraction starts from the kathode, that the break contraction starts from the anode;* in other words, that *the make stimulus is kathodic, the break stimulus anodic.* The experiments demonstrating this statement are as follows:—

(*Exp.* I.) Two levers rest upon a curarised muscle near its two ends, to which the kathode and anode respectively are connected, and are arranged against a recording surface; on making the current both levers rise, the kathodic a little sooner than the anodic; on breaking the current both levers rise, the anodic a little sooner than the kathodic.

(*Exp.* II.) A muscle is injured at one end and stimulated by make and break of a constant current, first in one, then in the opposite direction. It is found that when the kathode is at the injured end the make stimulus is less effectual than on the uninjured muscle; when the anode is at the injured end, the break stimulus is less effectual than on the uninjured muscle.

The statement made above applies to smooth as well as to striped muscle, although an apparent exception usually occurs in the former, and sometimes in the latter case, *i.e.* a contraction apparently started at the anode as well as at the kathode; on closer examination it is, however, found that whereas excitation starts from the precise point with which the kathode is in contact, it starts from an area at some distance surrounding the anode

(Biedermann). We shall encounter a similar phenomenon and shall give its explanation in dealing with the excitation of human nerve.

It is often extremely difficult in the examination of an excited muscle to determine whether a given portion moves actively or is moved passively by other portions. The difficulty may be overcome by painting distinct bars across the muscle; these will be seen to approximate in a contracted part, whereas they may be seen to separate in a stretched part.

Induced currents.—In the application of induced currents there is no direct connection of the battery with the muscle—the latter is connected with the *secondary* coil, and is stimulated by currents induced in that coil when the battery current begins and ceases to flow through the *primary* coil. The current which is induced in the secondary coil when the battery current begins to flow through the primary coil, is the make induced current; that which is induced in the secondary coil when the battery current ceases to flow, is the break induced current. These two currents are in opposite directions, and are not to be confused with the make and break of a constant current. They are of momentary duration, the beginning and end of each induced current being practically simultaneous, so that the stimulus of each is compounded of an instantaneous rise and fall of current. Induced currents are the most frequently employed test of excitability; their strength is varied by varying the distance of the secondary from the primary coil; in the case of muscle, for instance, excitability is determined by finding the greatest distance of secondary from primary at which response is obtained, or by observing increase or diminution in the height of contractions obtained, while the two coils remain at a distance previously determined to give a moderate strength of stimulation. Comparing the effects at make and break of the primary current, *i.e.* the effects of the make induced current and of the break induced current, it will be found that the contraction caused by the break induced current is stronger than that caused by the make induced current, or, what amounts to the same thing, that the contraction at break will be produced by a weaker current than the contraction at make. This is not a specific difference comparable with the differences between contractions provoked by make and break of a constant current, but simply an evidence of the fact that the break induction current is sharper than the make induction current. The two contractions can be equalised by modifying the connections of the primary coil according to the plan first used by Helmholtz (see p. 315).

A '*maximal*' stimulus is one which causes a muscle to perform the greatest contraction of which it is capable as the effect of a single stimulus; a stimulus of greater strength cannot therefore give rise to a greater effect. A '*submaximal*' stimulus is one which causes a muscle to perform a contraction smaller than that which is brought about by a maximal stimulus. A '*minimal*' stimulus is the weakest stimulus which will cause any contraction at all.

Myograph.—Each induction current gives a single muscular contraction or twitch, the form of which is studied by the graphic method. A lever in connection with a muscle, and rubbing against a travelling smoked surface so as to give a magnified record of the movements of the muscle, constitutes a *myograph*. Myographs are of many kinds and shapes, according to special requirements. The recording surface may consist of a cylinder made to revolve by clockwork; or of a plate on a carrier which is shot along horizontal guides by a spring; or of a plate fixed to a pendulum. In every case the rate of movement of the surface is to be determined by a *chronograph* marking time simultaneously with the movements of the muscle lever. A vibrating tuning-fork with a pen fixed to one of its prongs, or a vibrating reed interrupting the circuit of a small electro-magnet with a pen fixed to its armature, constitute the chronographs in most frequent use. A tuning-fork vibrating 100 times per second traces a series of teeth, each of which indicates $\frac{1}{100}$th second, similarly a reed vibrating 20, 50, 100, or 200 times per second, interrupting a current an equal number of times, traces the time-indications in $\frac{1}{20}$ths, $\frac{1}{50}$ths, $\frac{1}{100}$ths, or $\frac{1}{200}$ths.

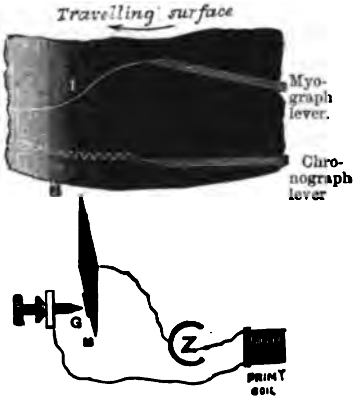


FIG. 132.

Fixed key opened by a recording cylinder, as used for taking a latent period. The point of stimulation is marked by touching the myograph lever with the peg in contact with the shut key; the lost time is ascertained from the interval between that point and the rise of the curve described when the recording surface has passed at full speed and struck open the key.

A simple contraction or twitch.—A single induction shock (make or break induced currents) led into a muscle, causes a single contraction or twitch. If, instead of producing the make or break in the primary circuit by a key moved by hand, this be done by a key which is closed or opened by a peg fastened to the travelling surface (cylinder or plate), it will be easy to observe that the muscle does not contract at the precise instant of stimulation, but a fraction of a second later. This interval between stimulation and effect is called the '*latent period*' or physiological lost time.

The length of the latent period in voluntary muscle is $\frac{1}{100}$th second (Helmholtz), $\frac{1}{200}$th second (Yeo), $\frac{1}{400}$th second (B. Sanderson). The last-named figure is the shortest obtainable under the most favourable conditions, and is not perceptibly longer than the latent period of the current of action.

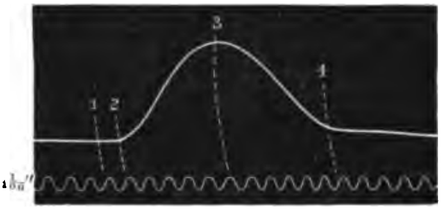


FIG. 133.—A SINGLE MUSCULAR CONTRACTION. (Frog's Gastrocnemius.)

From 1 to 2 is the latent period; from 2 to 3 the period of shortening; from 3 to 4 the period of relaxation.

The latent period is followed by the muscular contraction, which, when recorded as just described, consists of an ascending portion, during which the muscle shortens to a maximum, and a descending portion, during which the muscle returns to its original length. The total duration of a single muscular twitch is about $\frac{1}{10}$th second.

A muscle to which a weight is suspended is said to be '*loaded*;' if a support is so adjusted that the muscle raises the weight only during contraction, and is not stretched by the weight when at rest, the muscle is said to be '*after-loaded*.' If a muscle contracts against a small and constant resistance, so as to be extended by a constant force during its contraction, the curve described by a light lever attached to it is termed '*isotonic*.' If a muscle contracts against a large resistance, *e.g.* a strong spring, so that it can shorten very little, the curve described by a lever attached to it is termed '*isometric*.' The latter is flat-topped, *i.e.* exhibits a period of maintenance at maximum contraction. As ordinarily employed, the myograph gives an isotonic curve;

the isometric method is exemplified by the spring 'dynamometers' used for clinical purposes.

Summation.—If a muscle is made to receive two stimuli in rapid succession, the effects of each will be added together and produce a greater effect than either separately; the second contraction will be superposed upon the first. This is a summation of *effects*, as distinguished from summation of *stimuli.*

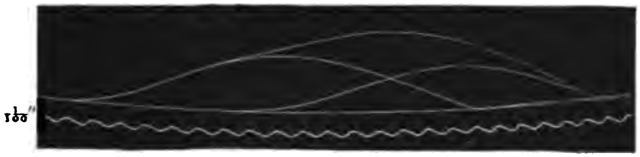


FIG. 134.—SUPERPOSITION OF TWO SINGLE CONTRACTIONS.

Each contraction is recorded alone by a break shock caused by opening a fixed key; both keys are then set, and the recording plate striking them open successively causes two stimuli and a summation of the two contractions.

If the two stimuli are in such close succession that the second occurs during the latent period of the first, the result will differ according as the stimuli are maximal or submaximal. If they are maximal, the contraction will be produced by the first stimulus, and will be unaffected by the second stimulus; if they are submaximal, the two stimuli will become added together and produce a greater effect than either separately. This is summation of stimuli.

A succession of stimuli will cause a succession of contractions, the number of contractions corresponding with the number of stimuli. As the frequency of these is increased, so the frequency of the individual contractions increases. The muscle now does not completely relax, but remains more or less permanently contracted, so that the point of the lever attached to it is kept above the level at which it would trace if the muscle were relaxed, and makes from this new level smaller excursions corresponding with individual contractions. This is incipient or incomplete tetanus, or, as it is sometimes called, '*clonus.*' With still further increase in the frequency of stimulation, the individual contractions become completely fused, the muscle remains in complete contraction so long as the stimulation is kept up, and the lever traces an unbroken line during this period. This is complete *tetanus.* The smallest frequency of stimuli required to produce it, varies between 20 and 50 per second for ordinary striated muscle, according to temperature and fatigue. Beyond this minimum any further increase of frequency (strength and quickness of stimuli remaining constant) gives no further increase in the amount of muscular shortening.

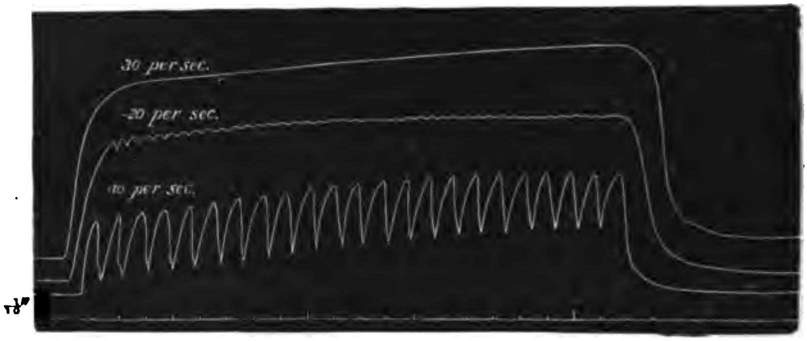


FIG. 135.—COMPOSITION OF TETANUS.

Stimuli caused by a spring interrupting primary circuit by vibrating in and out of a mercury cup; the vibration frequency is increased by shortening the spring (see also fig. 126.)

The contraction of striated muscle varies in different animals and in different parts of the same animal, and may be modified by fatigue, by temperature, and by drugs. In different animals, some muscles subserve short sharp movements, others prolonged movements; their individual contractions are correspondingly short or long; *e.g.* in the crayfish, the muscles that move the tail give short twitches, those that move the claw give long grasps; in the frog, the gastrocnemius gives a longer contraction than the hypoglossus; in the rabbit, the soleus (pale muscle) gives a longer contraction than the gastrocnemius (red muscle); in man, the muscles of the upper extremity give shorter contractions than those of the lower extremity.

A muscle which from any cause gives a long contraction, is tetanised at a lower stimulation frequency than a muscle giving a short contraction. Red muscle, cooled muscle, fatigued muscle have a lower minimum tetanising frequency than pale muscle or normal muscle.

Fatigue affects muscular activity, causing a diminution of absolute force, and of available work, and a general sluggishness of movement. The record of a series of muscular contractions exhibits the gradual development of the slowing and declining activity, after a short period of exaltation. The entire process of fatigue is divisible into two stages: (1) a short preliminary stage, during which the contractions increase in height and in duration; (2) a longer stage, during which they continue to increase in duration but progressively diminish in height. Figs. 136 and 137 illustrate these points, and fig. 138, given to show the effects of diminishing temperature, might equally well be an example of the two stages in a fatigue effect. According to Kronecker, the curve of decline in the contractions of an after-loaded frog's muscle stimulated at regular intervals, is a straight line.

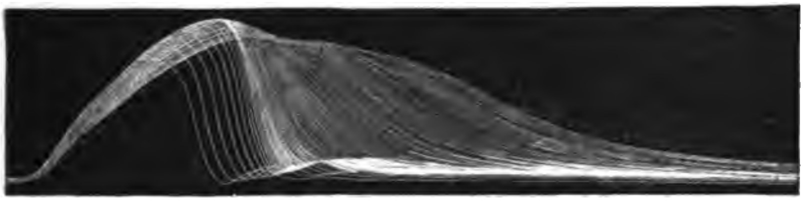


FIG. 136.—FATIGUE. (Frog's Gastrocnemius.)

Direct excitation; 125 successive maximal contractions at intervals of 1⅓ sec., showing at the outset increase of height and of duration, later decreasing height. (The exhaustion has not been pushed to the end).

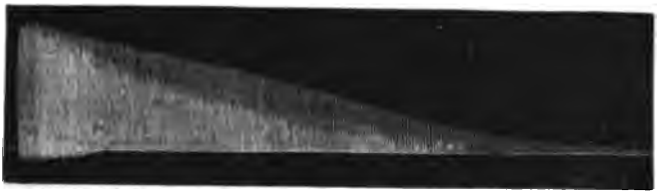


FIG. 137.—FATIGUE. (Frog's Gastrocnemius.)

About 250 make and break stimuli. (The recording surface travels very slowly, so that each contraction marks a vertical line only; the make disappear sooner than the break effects).

If left to itself, a muscle which has been exhausted—*i.e.* forced into action until it can act no longer—will recover; normally in the body a muscle is preserved from exhaustion, and even from appreciable fatigue, by the circulating blood bringing fresh matter and carrying off fatigue products. We shall see later (p. 378) that the exhaustion of muscle by nerve-action is rendered impossible by the comparative instability of the end-plates, but the point which we should now clearly recognise is that even an *excised bloodless muscle* has within itself, material and power of self-restoration after exhaustion, independently of new material furnished by the blood; left to itself, an isolated bloodless muscle recovers contractility.

A given muscle contracts more or less suddenly and sharply according as temperature is high or low. As the effect of cold the record of a single contraction exhibits (1) a longer latent period, a prolonged and a higher contraction, (2) a still longer latent period, and a still more prolonged, but lower, contraction. Thus, as might be expected, the effects of lowered temperature are identical with those of fatigue, and in both cases attributable to greater sluggishness of change. As the effect of increased temperature, each contraction becomes shorter and smaller; the excitability, after a slight increase, diminishes and is lost; finally, when the temperature exceeds 40°-50° C., the muscle shortens and becomes rigid (heat-rigor). In this rigor the shortening exceeds that produced by a maximal tetanus, but the absolute force of the contraction is very small.

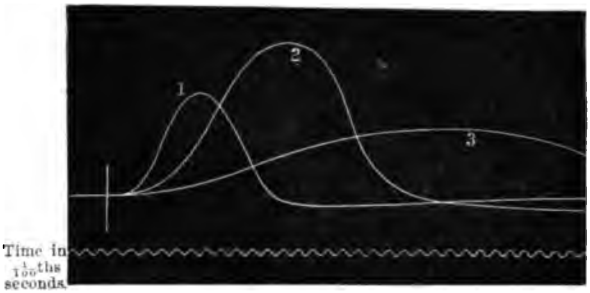


FIG. 138.—EFFECT OF TEMPERATURE UPON MUSCULAR CONTRACTION.

1. Normal. 2. Cooling. 3. Very cold.

A saline extract of exhausted muscle depresses the excitability of fresh muscle through the vessels of which it is made to circulate (Ranke). The blood of a dog exhausted by excessive exercise, causes 'symptoms of fatigue' if transfused into the vascular system of a fresh dog (Mosso). These effects are attributable to 'fatigue products.'

Among drugs causing a modification of contraction by their direct action upon muscle, the most notable is *veratrin*, which, if injected into an entire frog, or directly applied to an excised muscle, causes an excessive prolongation of the muscular contraction. Among inorganic bodies, the *calcium* salts may be mentioned as producing a similar though less-marked effect.

Proteid solutions nourish or fail to nourish ordinary muscle, just as they nourish or fail to nourish cardiac muscle; serum-albumin is 'nutritive,' egg-albumin and the digestion proteids (albumose and peptone) are non-nutritive, and the latter are actually 'poisonous.' (J. Brinck.)

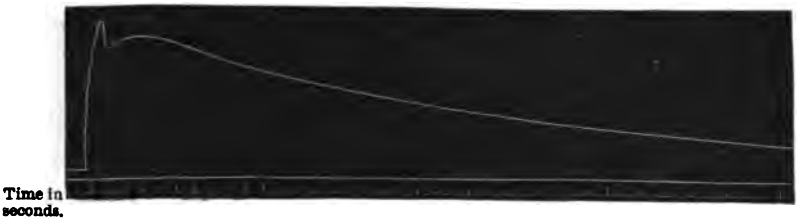


FIG. 139.—VERATRIN CURVE.

The muscular sound. Voluntary contraction.—Contracting muscle emits an audible sound; with a single contraction a short thud is heard; during a tetanic contraction a purring or rumbling noise is heard, having a pitch of about forty per second. But, as we shall see, this tone is no proof that impulses are generated with corresponding frequency, the pitch heard being in reality dependent upon the resonance tone of the listening ear. It is, however, stated that in muscular tetani produced by high stimulation frequencies (1,000 Bernstein, 700 Lovèn), a note of corresponding pitch, or of the next octave below, is audible; in observations of this kind it is necessary to guard against a fallacy due to the static effects of alternate charge and discharge; these, if they should occur, will cause an audible tone corresponding with the interruption frequency, but independent of any muscular contraction and equally well heard on dead muscle (Lovèn). The fallacy is obviated by touching a moist surface of the animal with a moist finger during the auscultation.

Every voluntary contraction, even the shortest, is considered to be a tetanic series of impulses; nevertheless it is possible to make a single voluntary contraction as short as a single induction twitch, or to cut it even shorter by the antagonist contraction. Wollaston, who first studied voluntary muscular contraction by the acoustic method, came to the conclusion that the muscle-note emitted during voluntary contraction has a vibration frequency of 36 per second. Helmholtz, by means of consonating springs, concluded that the actual number of neuro-muscular impulses producing this effect is 18 per second; and he pointed out as a fallacy of the acoustic method that the pitch of the sound depends, not upon the observed muscle, but upon the observer's ear, of which it is a resonance tone. Lovèn called attention to the fact that strychnia spasms in the frog have a rhythm of 8 to 10 per second, and considers this to be the normal rate of spinal discharge.

The maximum number of *double* (*i.e.* to *and* fro) voluntary movements which we can make in 1 second is 8 to 10; the smallest interval at which two separate motor impulses can be made to succeed each other is ·05 to ·06; the rhythm of morbid spasms—trepidation, clonus, tremor—is 8 to 10 per second, so also is that of clonic tremors occurring in the normal muscle, especially in the condition of fatigue or of shivering; and it has more recently been pointed out by Schäfer and by v. Kries that the graphic record of even the steadiest voluntary movement exhibits a tremor of about the same frequency (8 to 12). The sum of these various items signifies to us that the physiological mobility of the central nervous system is characterised by the maximum impulse-frequency 16 to 20 per second, or by the minimum impulse-interval ·05 to ·06 second.

Is the heart beat a long twitch or a short tetanus? We are now in a position to answer this question, and the state of our knowledge is such that the answer can be placed on surer ground than at a time when it rested upon interpretations of secondary contraction and of tetanic bruits. We need only very briefly consider these two data. (1) When the nerve of a nerve-muscle preparation is laid across the beating heart, the muscle gives a single twitch, at the outset of each beat, and occasionally also at its close; this was received as an indication that the heart's contraction is single and not multiple, and we shall find in a further section that this evidence is much strengthened by our present knowledge of its meaning; it is an index of the diphasic variation which accompanies each single contraction (p. 387). (2) The sound made by the contracting heart was formerly much quoted in support of the opposite view, according to which the systole was considered to be a short tetanus. The argument was as follows:—muscular sounds are due to a tetanic succession of impulses, the heart gives a sound during its contraction, therefore that contraction is tetanic. But we now admit that any contraction, even a single twitch, gives a sound, short if the contraction is short, long if the contraction is long; the major premise, and with it the argument itself, falls therefore to the ground. We can no longer hesitate to admit that each contraction of the ventricles is a single spasm; comparing the contractions of striated muscle, of cardiac muscle, and of smooth muscle, we recognise that the only difference is one of duration; the latent period, the rise and fall of contraction, maintain their relation to each other, and—in the cases of skeletal and of cardiac muscle—the passage of a single wave of change has been followed from origin to end along the excitable tissue—electrically, as we shall see on p. 387, and also mechanically, as is illustrated above.

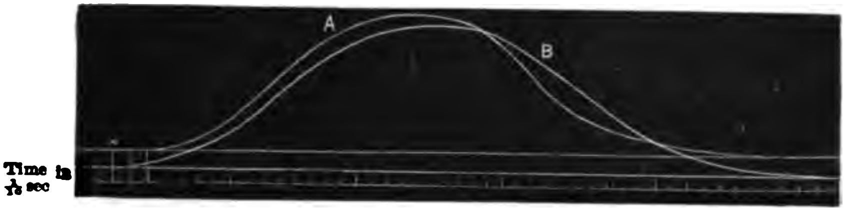


FIG 140.—WAVE OF CONTRACTION IN FROG'S VENTRICLE, TAKEN BY TWO LEVERS RESTING UPON IT NEAR THE APEX AND NEAR THE BASE.

Excitation x near base, *i.e.* in imitation of the normal origin of the contraction, marks the moment of excitation. The contraction of the base begins sooner and lasts longer than that of the apex.

Strength; work.—The *absolute strength* of a muscle is measured by the weight which a muscle just fails to lift on being stimulated, the weight being applied as an 'after-load.' This weight varies with the sectional area of muscle, not with its length; *i.e.* the absolute strength of a thick muscle is greater than that of a thin muscle; and the absolute strength of a long muscle is the same as that of a short muscle, if both are of the same thickness. The absolute strength of tetanised frog's muscle has been found to be about 3 kilogrammes per 1 square centimeter sectional area; of human muscle it is greater, viz. 5 to 10 kilogrammes per 1 square centimeter. This is for voluntary contraction; the strongest possible artificial tetanus only reaches ½ to ⅔ of the voluntary maximum. The absolute strength in tetanus is about double that of a single contraction in the frog, and no less than ten times its value in human muscle (Fick).

The *work done* by a muscle is measured by the product of weight raised × height. A muscle which shortens 10 millimeters raising a weight of 100 grammes, does work equal to

1,000 gramme-millimeters or 1 grammeter. Leaving out of account the weight of the muscle itself, no work is done when muscle contracts without raising a weight or overcoming some resistance. A tetanised muscle does work only at the beginning of tetanus, when it raises a weight; during the tetanus, while the weight is kept up, the contraction is static and no work is done. If we measure the work done by a muscle made to raise a succession of increasing weights, we shall find that the work done increases to a maximum, from which it declines with further increase of weight.

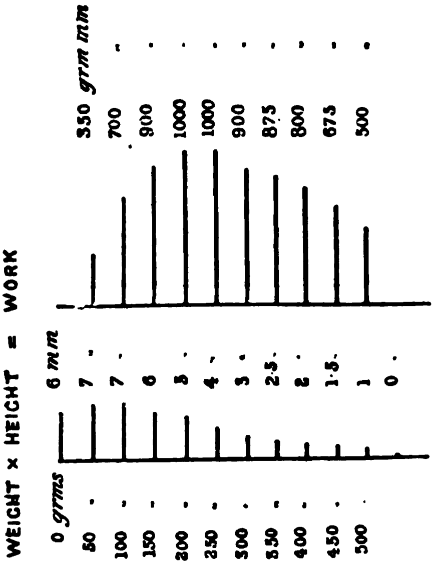


FIG. 141.

Work done thus depends upon three factors—(1) amount of weight whether as 'load' or as 'after-load'; (2) length of muscle; (3) sectional area of muscle. Length × sectional area are equivalent to bulk or weight; the maximum work which can be done is therefore dependent upon the bulk or weight of the muscle in action. It has been found that for frog's muscle this maximum under favourable circumstances is in a simple contraction nearly 1 grammeter per 1 gramme, and in a short tetanus about 4 grammeters per 1 gramme.

An ordinary labourer at work does about $\frac{1}{8}$ grammeter per gramme muscle per second, *i.e.* taking his muscle to be 20 to 25 kilogrammes, his work during 8 hours =115,000 to 144,000 kilogrammeters. A man during an ordinary walk does work at about the same rate. A long-distance bicycle racer was calculated to do work for 8 hours at the rate of 1 grammeter per gramme per second, the weight of his muscle being estimated at 25 kilogrammes; a rowing man was calculated to work at the same rate (1 grammeter per gramme per second), but only for a short time; the work of a short-distance runner has been estimated at between 2 and 2·5 grammeters per gramme per second. According to Marey the work done in walking and running on level ground amounts to between 10 and 20 kilogrammeters per step.

The muscular strength on man is tested by means of the *dynamometer*, which in its ordinary clinical form consists of a strong oval spring to be grasped in the hand, the value of the flattening being shown by an index and scale graduated in pounds or kilogrammes. The value of the instrument is much diminished by the fact that habit and 'knack' are very important factors in the maximum squeeze: its indications are of greater value if the instrument is converted into a *dynamograph*; the manner of maintenance of a prolonged maximum effort for regular periods, or the character of a series of maximum efforts for regular periods, may then be recorded on a slowly travelling surface, *e.g.* a cylinder on the hour axis of an ordinary clock; and from such records an estimate may be formed of the muscular strength, of its rate of decline in a succession of efforts, and of its rate of recovery from such decline.

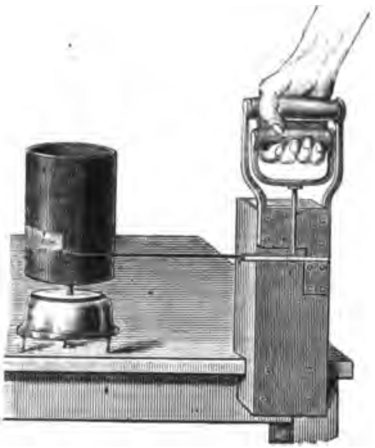


FIG. 142.—DYNAMOGRAPH.

Short straight spring and long lever (represented here much shorter than it is in reality).

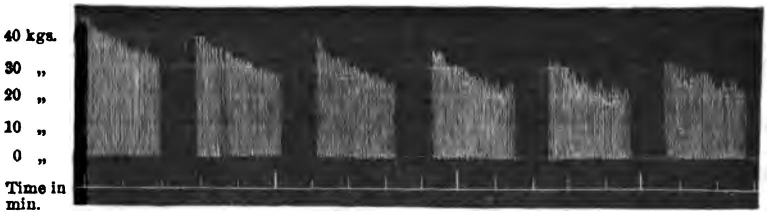


FIG. 143.—DYNAMOGRAPH TRACING.

Each group of lines is the effect of 30 maximal efforts, each lasting two seconds. Intervals of rest for one minute between successive groups.

By means of an instrument devised by Mosso and termed by him the *ergograph*, similar estimates may be made, with the advantage that they may be numerically expressed in terms of work as kilogrammeters, although in other respects the isometric method is preferable. The half-supinated arm is attached to a horizontal support, a cord from a ring round the middle finger passes over a pulley and carries a weight, the hand is kept in position by two tubes into which the index and ring fingers are inserted; the successive elevations of the weight by flexion of the middle finger are recorded in the usual manner.

The three lever systems.—The mechanical disposition of the muscles, tendons, and bones of the animal body presents examples of the three fundamental lever systems. As instances of the first system, in which the *fulcrum* is situated between the *power* and the *weight*, may be mentioned, the action of the triceps brachii in the extension of the forearm, that of the hamstring muscles in raising the body from a forward stoop, that of the calf muscles in the movement of pointing the toe; as an instance of the second system, in which the weight is placed between the fulcrum and the power, may be mentioned the action of the calf muscles in raising the body on tiptoe; as instances of the third class, in which the power is applied to a lever between the fulcrum and the weight, may be mentioned the actions of the biceps upon the forearm, of the hamstrings upon the leg, of the temporal and masseter muscles upon the lower jaw. Levers of the second system afford increase of *power* at the expense of quickness and range of movement, the power-arm of the lever being longer than the weight-arm, as is illustrated in the mechanism of a nut-cracker; levers of the third system afford increased *quickness* and range of movement at the expense of power, the weight-arm of the lever being longer than the power-arm, as is illustrated in the use of a fishing-rod; levers of the first kind may afford either of these characters at the expense of the other, according as the distance F P is greater or smaller than the distance F W; generally, however, the mechanical conditions in the body are such that this system affords quickness

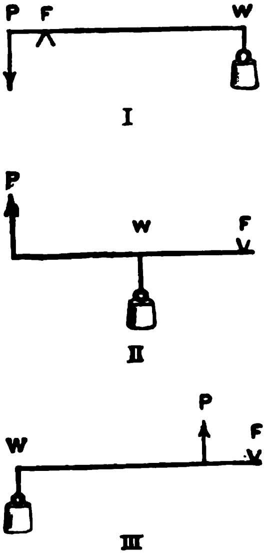


FIG. 144.

levers rather than power levers. The fuller and more detailed consideration of the principal lever movements of the body in various circumstances belongs to applied anatomy rather than to physiology.

Co-operative antagonism.—It is a fundamental principle common to the neuro-muscular actions of the body, that the normal voluntary movement of any given group of muscles is usually associated with *contraction* of the antagonistic muscles. This physiological principle of 'co-operative antagonism' may be easily realised by simple observations, is illustrated in familiar pathological occurrences, and offers analogies outside the domain of medicine, beyond which we shall, however, not pursue it. To take a simple and easily observed case, we may refer to the flexors and extensors of the fingers; if the fingers of one hand be flexed and the forearm félt by the other hand, it will be noticeable that the contraction of the flexor muscles is accompanied—not by relaxation—but by *contraction* of the extensors; and when the fist is clenched, it will be still more obvious that contraction of the flexors is accompanied by *contraction* of the extensors.

That to the effective action of a muscular group the effective action of opposed muscles is necessary, is well illustrated in *lead-palsy*; in a typical case of this affection the hand drops at the wrist in consequence of paralysis of the extensor muscles; the flexors are not paralysed, but movements of flexion cannot be carried out; conversely, cases are met with of muscular paralysis limited to the flexor group of forearm muscles, when not only flexion, but also extension become impossible—*i.e.* to the due execution of a measured movement either of flexion or of extension, the integrity of the antagonists as well as of the direct motors is necessary; or otherwise, antagonistic muscles co-operate in the execution of movements, now one, now the other group exercising the major or predominant power. This is the rule, but there are exceptions to it; in very rapid movements, and in movements against an insuperable external resistance, the contraction of groups of muscles is not accompanied by any contraction of the antagonists. It is a subordinate although obvious feature of any extensive movement, that in addition to the *active* participation of antagonists, these must also undergo a *passive* elongation, calling into greater play their physical property of elasticity, and thus contributing to the steadying effect which is an essential condition of all delicate adjustments.

Heat evolved.—The chemical action taking place in muscle is of course accompanied with an evolution of heat, and its amount is increased during contraction. It has been found that, *cæteris paribus*, (1) more heat is evolved in the contraction of a stretched than in that of an unstretched muscle, (2) more heat is evolved by a muscle which contracts without doing work, than by a muscle which does work (Heidenhain). These facts have a far deeper significance than is superficially apparent. The first fact implies that pure muscle is not a mere machine discharging energy irrespectively of the work to be done, but that it evolves much or little energy according as it pulls against much or little resistance, and it is obvious that this relation between demand by tension and response by action is an important feature in the economy of natural contraction. The second fact is an illustration of the conservation of energy: if the total energy set free appears in the form of heat, there is more heat than if some of the energy goes off as work. The most favourable conditions for the demonstration of the heat of muscular contraction are therefore established by tetanising stretched muscle which cannot shorten and do work. A frog's gastrocnemius so treated will show a rise of about ·1° at the end of a minute. A single contraction is attended with a rise of about 0·002°.

Some idea of the amount of heat evolved by muscular contraction may be arrived at by comparing the temperature of the venous blood coming from tetanised muscles with that of arterial blood. If, for instance, through a given group of muscles 100 c.c. of blood has passed per minute, and has been raised to a temperature 0·2° above that of arterial blood, it follows that heat has been produced at the rate of 20 calories per minute in the muscles in question. Such an estimate does not, however, give the total amount of heat evolved; to it must be added the value of any rise of temperature of the muscle itself; if, for instance, the muscle in action weighs 50 grms. and its temperature is raised 0·1°, this value will be about 5 calories—to be added to the 20 calories as above estimated. And even then we have left out of account the heat dissipated by radiation from the muscle.

Direct estimations of the amount of heat evolved have been obtained on excised frog's muscles, and on mammalian muscle after the circulation has been arrested. Fick estimated that frog's muscle evolves 1 to 3 milli-calories per 1 gramme in a single contraction. Ludwig gives for dog's bloodless muscle a heat-production of 1 milli-calorie per gramme per contraction. It is probable that these values are below the value of normal heat-production of muscle in the body, more particularly in the case of mammalian muscle, which rapidly runs down after arrest of the circulation.

Curare is the drug most frequently spoken of in association with the muscle and nerve. A curarised frog lies motionless and paralysed, yet its muscles are excitable, and so are its nerves ; a curarised cat, or dog, or rabbit, is equally paralysed, and dies by arrest of respiratory movements unless artificial respiration is employed. The fundamental experiment demonstrative of the action of curare is as follows :—a drop of a one per cent. solution is injected under the skin of a frog, and when the animal is found to be completely paralysed, it is pithed and the sciatic nerve is exposed, or a nerve-muscle preparation is put up as shown in fig. 131. Excitation of the nerve produces no effect, while the muscles are as excitable as before. By other experiments it may be shown that the nerve retains excitability, *e.g.* the negative variation persists as before. Seeing that the muscle is excitable, that the nerve is excitable, but that excitation of the nerve fails to put the muscle in motion, it is inferred that curare acts upon the junction between nerve and muscle, *i.e.* that it causes a block at the motor end-plates. It may be shown by a variation of the experiment that curare has practically no action upon sensory fibres or cells. A frog is curarised as before, but one limb is protected by a tight ligature leaving out the nerve; when the paralysis is complete it will be found that cutaneous stimuli on any part of the curarised frog can cause reflex movements of the protected, and therefore uncurarised, limb.

CHAPTER X

THE PERIPHERAL NERVOUS SYSTEM. NERVE

PAGE
314 Classification and terminology—Minute structure.
349 Chemical composition.
350 Section and excitation—**'Law of specific nervous energies'—'Law of isolate** conduction.'
352 **Consequences of nerve-section**: (1) Paralysis—(2) Loss of excitability—(3) Degeneration—(4) Regeneration—(5) Restoration of function and of excitability.
352 **Degeneration**: of mixed nerve—of anterior root—of posterior root—'Trophic centres'—Immediate restoration (?)—Recurrent sensory fibres.
355 * **Trophic nerves** (?).
356 **Stimuli**: Evidence of stimulation—Movement—Sensation—The current of action—Natural and artificial stimuli—Excitability and conductivity.
360 * **The constant current**: Make and break contractions—Pflüger's 'law' of contractions—Ritter's tetanus—Formula of contractions on man—Reaction of degeneration.
366 * **Electrotonus**: Electrotonic currents—Electrotonic alterations of excitability The paradoxical contraction—Experiments on man—Experiments on sensory nerves.
373 **Velocity of nervous impulses**: In motor nerves of man—of frog—In sensory nerves (?)—In sympathetic nerves (?)—Velocity of negative variation.
375 Conduction in both directions—Paul Bert's experiment—Du Bois-Reymond's experiment.
376 Inequalities of excitability—At different points—Of different fibres. Avalanche theory—The Ritter-Valli 'law'—In motor nerves—in sensory nerves.
377 **Fatigue** of nerve—of muscle—of the motor end-plate.

Classification and terminology.—Nerves and nerve-fibres are classified from several points of view—(*a*) according to their obvious source and course, as *cerebro-spinal* and *sympathetic*; (*b*) according to their microscopical structure, as *medullated* and *non-medullated*; (*c*) according to their embryonic origin and distribution, as *somatic* and *splanchnic*; (*d*) according to their function, as *efferent* and *afferent*. And we shall learn shortly that these divisions are subdivided into several varieties according to the kinds of impulses conveyed. As regards the correspondence of the various kinds denoted by these terms, it is to be remarked,

(1) that cerebro-spinal nerves are in major part composed of medullated fibres, in minor part of non-medullated fibres, while sympathetic nerves are in major part composed of non-medullated fibres, in minor part of medullated fibres; (2) that both medullated and non-medullated fibres may be either afferent or efferent, there being here no correspondence between difference of structure and difference of function. The interchange of fibres between the two classes of nerves is by the *rami communicantes* through which the cerebro-spinal nerves receive grey fibres from the sympathetic system and give to that system white fibres. But, as we have already seen, no hard and fast line of distinction is to be drawn between the two systems. Sympathetic nerve-fibres have their centres in the spinal axis and not in their own ganglia.

A certain amount of correspondence is presumed to exist between the size of fibre and the nature of its function. As a rule, the largest nerve-fibres are those distributed as motor fibres of skeletal muscle; fibres in the posterior nerve-roots and in the posterior columns of the cord are on the average of inferior calibre to fibres in the anterior roots and in the pyramidal tracts. Another difference has already been alluded to under the physiological anatomy of cardiac and vaso-motor nerves, where we saw that these are characterised by their very small diameter (2 to 4μ), and stated that in their course along the peripheral nerves, vaso-inhibitory fibres are medullated while vaso-augmentor fibres are non-medullated.

Medullated or white nerve-fibres owe their name to the medulla or myelin, which is a fatty sheath surrounding the cylinder-axis. From within outwards a fibre of this kind consists of—(1) axis-cylinder; (2) medullary sheath or white substance of Schwann; (3) primitive sheath or neurilemma.

The axis-cylinder is an unbroken filament of protoplasm extending from centre to periphery, and is the essential or conducting part of the fibre.[1] The medullary sheath is a string of hollow cylinders of a fatty nature surrounding the axis-cylinder, and joined end to end by cement substance at 'nodes' (Ranvier); this is an indication that each bit of medullary sheath between two nodes constitutes a single cell, a view which is borne out by the fact that each such bit or inter-node possesses one and only one nucleus. The neurilemma is to the nerve-fibre what the sarcolemma is to the muscle-fibre, viz. a delicate membranous sheath enclosing its substance. Outside this a second membranous sheath is commonly visible enclosing solitary nerve-fibres; this is Henle's sheath, and is not an integral part of the fibre, but a prolongation derived from the connective tissue (perineurium), by which nerve-fibres are held together in bundles.

---

[1] According to Engelmann the axis-cylinder also is segmented.

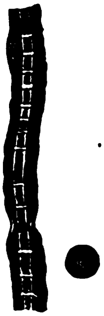


Fig. 145. Transverse and longitudinal sections of a medullated nerve fibre.

Fig. 146. Longitudinal optical section of a group of non-medullated fibres.

A 'non-medullated,' 'pale,' or 'grey' fibre is nerve reduced to its simplest expression—a naked axis-cylinder. It is to be regarded as being less highly developed than medullated nerve, for it exists in greatest abundance in visceral nerves, in association with non-striped muscle, and histologically, in addition to its simpler structure, it is characterised by the presence of numerous nuclei.

Motor and *efferent*—*sensory* and *afferent* are not completely synonymous pairs of terms. All motor nerves are efferent, but all efferent nerves are not motor; some are anti-motor or 'inhibitory' of motion. All sensory nerves are afferent, but all afferent nerves are not 'sensory' in the exact acceptation of the term 'sensation,' 'sensory' being strictly applicable not to all centripetal impressions, *but only to such as excite consciousness.* Many, if not all afferent channels, may however on some occasions convey impulses which reach consciousness, while habitually conveying impulses of which we remain unconscious. Normally we are not conscious of the beating of the heart, nor of digestive actions; in disease we may become painfully conscious of them. On the other hand all, or at least most, sensory channels may on some occasions convey impulses of which we remain unconscious though habitually we perceive them. A man may fail to perceive that he has received a serious injury if his perceptive centre is preoccupied by a sufficiently powerful idea or sensation. As regards the distribution of these several kinds of nerves, cerebro-spinal nerves are distributed for the most part to the skin and to voluntary muscles, skin-nerves being mostly sensory in function, muscle-nerves being mostly motor in function. The skin, however, contains a small proportion of unstriped muscle which receives motor nerve-fibres derived from the sympathetic; and voluntary muscles, or more precisely their tendons and sheaths, possess also a small proportion of sensory nerves, through which the sensorium is kept informed of their state. Motor nerve-fibres are also distributed to internal organs; the impulses which they convey are, however, independent of the will; by voluntary effort we cannot directly move the involuntary muscle of such organs.

Nerve-fibres may be classified as follows:—

AFFERENT		olfactory	cutaneous sensory
		optic	muscular sensory
		gustatory	visceral sensory
		auditory	? thermic sensory
		tactile	? pathic
EFFERENT	MOTOR	musculo-motor	to *skeletal muscle*
		vaso-motor	to *cardiac muscle* (*accelerators*) to *arterial muscle* (*constrictors*)
		viscero-motor	to *intestinal muscle*
		secreto-motor	to *gland cells*
		? 'thermogenic' and 'trophic'	to *all tissues?*
	INHIBITORY	vaso-inhibitory	to *cardiac muscle* (*inhibiting*) to *arterial muscle* (*dilating*)
		viscero-inhibitory	to *intestinal muscle*

There is as yet no proof of direct voluntary inhibition at the periphery; voluntary inhibition of a peripheral action occurs at the centre whence the action would have been excited in the absence of inhibitory control. Of involuntary motor paths we have proof in the action of nerves upon arterial muscle and upon secretory glands; both these are entirely exempt from direct voluntary influence; all that we can voluntarily effect is to apply a peripheral stimulus which will influence them by a reflex mechanism. *Vaso-constriction* is a motor effect; *vaso-dilatation* is of an inhibitory nature; we do not know, however, whether the seat of inhibition is in the muscular element itself, or in some hypothetical peripheral centre contained in it. It is analogous with the better-known case of *cardiac inhibition* by the *vagus*, but in this case also we do not know whether the motor action is interfered with in the motor element itself, or in an intermediate nerve-element—the ganglion-cell. Closely analogous with vaso-motor and vaso-inhibitory nerves, but still less completely understood, and indeed less well certified by experiment, are the effects upon *intestinal movements* of impulses passing to them through efferent channels. Intestinal movements may through such channels be *excited* or *arrested*; usually the result of *vagus* excitation is increased movement, of *splanchnic* excitation diminished movement; but such results are not infallibly obtained, being dependent upon a variety of circumstances (see p. 163).

Secreto-motor fibres are subdivided into two varieties; 1, such as accelerate the discharge of water; 2, such as accelerate the discharge of the *protoplasm-product*, which is to form the essential constituent of the secretion. These latter secreto-motor fibres are distinguished from the former as 'trophic,' a term which is not free from objection, seeing that such fibres have not been proved to excite cell-nutrition, though they certainly effect the converse, viz. cell-disintegration (see p. 178).

Afferent nerves are naturally classified in accordance with their obvious functions as *olfactory*, *optic*, *acoustic*, *tactile*, and *common sensory*. There are less obvious and less satisfactory reasons for admitting a further classification of nerve-fibres into *thermic* and *pathic*, for the proof that impressions of *heat*, of *cold*, and of *pain* are specific and served by separate fibres distinct from common sensory fibres, is not completely clear and unassailable. The term 'sensory' is in common use and cannot be advantageously ignored; it is well, therefore, to recognise clearly that the same nerve or the same nerve-fibre may at one time be truly sensory, inasmuch as it may be the channel of a peripheral stimulus which excites consciousness, while at another time it may be only the channel of an impulse which effects a reflex act in the absence of consciousness. There is no reason for believing that reflex acts are effected through nerve-fibres, afferent or efferent, other than those which convey voluntary and sensory impulses; the same afferent and efferent fibres as those which convey impulses going on to the brain, convey reflex involuntary impulses (which may or may not be perceived) to and from the spinal cord. Further, it may be repeated that whereas some nerves usually carry an impulse to its supreme end as a sensation, while others usually carry impulses short of this, so that 'sensory' is the term applied to the former, 'afferent' to the latter—yet the distinction thus implied is not real, for any such habitually ‘sensory’ nerve may on occasions be merely afferent, and *vice versâ* any such habitually ‘afferent’ nerve may on occasions be sensory.

The classification into ‘splanchnic’ and ‘somatic’[1] is derived from the corresponding embryological terms denoting the two layers of the mesoblast which respectively become viscus and body-wall. The terminology, as applied to nerves, does not imply that they are developed from the splanchnic and somatic layers of the mesoblast (all nerves, cerebro-spinal and sympathetic alike, being outgrowths from a central axis which is epiblastic), nor even that they supply tissues which are derived from these two layers respectively, seeing that a ‘somatic’ tissue, *e.g.* the skin, receives ‘splanchnic’ (vaso-motor) as well as somatic (sensory) nerves.

The origin of the terms as used by Gaskell is as follows:—*a.* The vascular, intestinal and glandular nerves were classed under the designations ‘visceral’ or ‘splanchnic.’ *b.* Embryological descriptions were taken to justify the recognition of Bell's respiratory system of nerves (facial, phrenic, intercostals, spinal accessory) as ‘splanchnic,’ and as being derived from a separate ‘lateral’ root, supplying the lateral or ventral plates of the mesoblast (which form part of the somatopleure, as well as of the splanchnopleure) as distinguished from the axial or dorsal portion forming the mesoblastic somites. *c.* This lateral ‘root hypothesis’ was extended to the whole cord and brain, and made to include all vascular, visceral, and glandular nerves. Thus Gaskell's ‘somatic nerves supply parts derived from the epiblast and from the mesoblastic somites,’ his ‘splanchnic nerves supply parts derived from the hypoblast and from the rest of the mesoblast.’ The latter comprise the vascular, visceral, glandular, and respiratory nerves.

The chemistry of nerve is very imperfect, and from a physiological standpoint very insignificant—no differences having ever been detected between living and dead, or between rested and exhausted nerve. The only point which appears to be established is that normal nerve-matter is faintly alkaline, while immediately after death it is found to be acid; it is probable, though not proved, that acidification also takes place during life in the cerebral grey matter, as a consequence of activity.

Our scanty knowledge of the subject is based upon analyses of the white matter of the brain, and upon micro-chemical reactions. From the first source it has been ascertained that ‘nerve-fat’ is of a peculiar composition, and that it contains cholesterin, lecithin, cerebrin, and protagon. *Cholesterin*, with which we have become acquainted as a constituent of bile, forms at least one half of this so-called fat, and the coincidence recalls to mind the every-day experience that liver-action has influence upon brain-action. No definite relationship has however been determined, and the supposition that the blood can be overcharged with cholesterin so as to give rise to a definite group of symptoms (cholesteræmia) has not been verified.

---

[1] σπλάγχνον, viscus; σῶμα, body.

Lecithin is the essential constituent of the so-called 'myelin' or white substance of medullated nerve, which is fixed and blackened by osmic acid.

Cerebrin is the name given to the indefinite phosphor-free body or group of bodies obtainable from brain-matter, probably by decomposition of 'protagon.'

The crystalline phosphorised body discovered by Liebreich and termed *protagon*, but considered by Hoppe-Seyler as a mixture of cerebrin and lecithin, is probably a compound of these bodies, *i.e.* a true proximate principle (Gamgee).

Kühne has described, under the name of *neurokeratin*, the reticular formation which he found to pervade the medulla of nerves, and to resist the action of the digestive ferments. The *neuroglia* of nerve-centres is of a similar character.

Analysis of the white matter gives on the average:—

Water			70 per 100
Solids	cholesterin	15·0	30 ,,
	proteids	7·5	
	lecithin	3	
	cerebrin	3	
	etc.	1·5	

The function of a nerve is ascertained by the observation of the alterations consequent upon (1) its *section*, (2) its *excitation*, such excitation being applied to the central and to the peripheral cut ends. The immediate consequence of nerve-section is 'paralysis'—in the case of motor nerves, inability to move the muscles served by the cut nerve—in the case of sensory nerves, inability to perceive sensations from the sensory district served by such nerves. All nerves may convey *occasional* impulses; some nerves are *constantly* engaged in the conduction of centripetal or centrifugal impulses, and the actions thus effected are spoken of as *tonic*. An instance of such tonic actions in the case of an efferent nerve is furnished by the cardiac fibres of the pneumogastric, in the case of an afferent nerve by the pulmonary fibres of the same nerve. If nerves which convey such tonic influence be divided, the effect is to cut it short; thus after section of the pneumogastrics the heart's beat is accelerated, the respiratory movement is slowed; these results, taken in conjunction with the confirmation obtained by excitation of the central and peripheral ends of the nerve, justify the conclusion that it conveys tonic influence to the heart which restrains its action, tonic influence from the lung which accelerates respiratory action at its seat of government—the spinal bulb.

The proof of the function of a nerve is completed by excitation, which is to be successively applied to the two ends of the divided nerve. In the case of most nervous impulses, which are not tonic but only occasional, excitation after section, and not section alone, furnishes the proof of function. Excitation of the peripheral end of a nerve, followed by an effect at the periphery, proves that the nerve contains efferent fibres, and the kind of effect at the periphery, whether motor or inhibitory or vaso-motor, shows what kind of efferent fibres the nerve contains. The absence of effect at the periphery proves the absence of efferent fibres; if such absence of effect is witnessed on a freshly divided nerve, efferent fibres are really absent from the normal nerve; if it is witnessed on a diseased nerve, or on a nerve divided some time previously, efferent fibres are *functionally* absent from the nerve, which has been rendered abnormal (degenerated) by previous interference or by disease. Excitation of the central end of a nerve, followed by movements expressive of sensation, or by vaso-motor reactions, proves that the nerve contains afferent fibres.

It is known from observations made upon man that excitation of the central cut end of a sensory nerve excites in consciousness the kind of sensation which that nerve habitually subserves. This is what is meant by the term '*law of specific nervous energies.*' A second important fact in nervous action, viz. that nerve-fibres constitute uninterrupted channels between central and peripheral organs, isolated from adjacent fibres, is spoken of as the '*law of isolated conduction.*' Both these 'laws' are implied in the familiar phrase 'each nerve-fibre minds its own proper business.' In general it is excitation of the central cut end of a nerve which excites sensation, excitation of the peripheral end being unfelt. But the rule is not absolute, the peripheral ends of many mixed nerves contain sensory fibres along which the impulses run towards the periphery before returning to their central destination. Such afferent fibres are known as *recurrent sensory fibres*; they are demonstrable in the peripheral end of the divided anterior root of spinal nerves and in the peripheral ends of mixed nerves (pp. 355, 475).

The consequences of nerve-section.—Division of a nerve has for its consequences in order of time (1) *paralysis* of motion or of sensation or of both, according as the nerve cut is motor or sensory or mixed; this paralysis is immediate and local; (2) *loss of excitability* of the nerve, coming on gradually and becoming complete within a few days, direct muscular excitability persisting for an indefinite period, especially to the galvanic current; (3) *degeneration* of the peripheral end of the nerve, also a gradual process, visible within a day or two, well marked at the end of three or four days, complete in about ten days; (4) *regeneration* of the previously fully degenerated peripheral end of the nerve, a still more gradual process, commencing indefinitely, but clearly visible about a month after the lesion has been produced, requiring from three to six months to complete itself, and then leading to (5) *restored motility*, *sensibility*, and *excitability*. These statements refer to the results of experiments upon warm-blooded animals; upon cold-blooded animals the last four stages are much more slowly consummated; upon young warm-blooded animals, on the contrary, the processes are accomplished more rapidly.

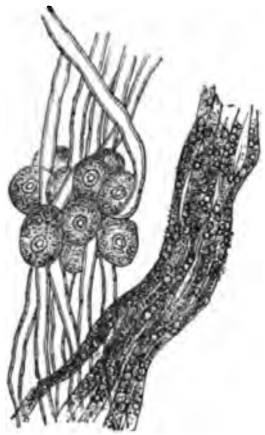


FIG. 147.

Groups of fibres from the anterior and posterior roots several days after section of both roots close to the cord; the anterior fibres are degenerated, the posterior are normal. (From an unpublished drawing by A. Waller, 1852.)

Trophic action of nerve-cells upon nerve-fibres.—*Wallerian degeneration.* The degeneration of nerve after section is a coarse and easily recognised change; hence the practical value of the method in the investigation of the distribution of nerves. A mixed nerve degenerates down to its ultimate distribution in muscle or in skin; the process is simultaneous throughout the length of the nerve, and does not gradually descend towards the periphery, there being no difference recognisable between fibres in a nerve trunk near and far from the section; according to Ranvier, the earliest signs of change are detected in the intramuscular nerve-ends. The rapidity with which the process takes place varies with the activity of tissue-life—*e.g.* it is more rapid in a young than in a full-grown animal, in a cold-blooded animal kept at high temperature than in one kept at a low temperature, in a healthy than in an enfeebled animal. The histological features are significant of excessive rather than of deficient metabolism, the nerve-cell being, so to speak, the nurse of the nerve-fibre, so that if the fibre is separated from the cell, it runs riot and destroys itself. The entire process is naturally divisible into two stages (1) the period preceding the loss of excitability, *i.e.* under ordinary circumstances up to about the third or fourth day; (2) a succeeding period of three or four weeks. During the first period the signs are those of increased activity—hypertrophy of protoplasm, hypertrophy and multiplication of nuclei, causing interruptions of the medullary sheath and of the conducting medulla itself. During the second period absorption of the broken-up fibres takes place, leading to their complete disappearance, and leaving nothing but a strand of connective tissue, which probably includes the actual primitive sheaths of the vanished fibres. Regeneration—the first signs of which are visible during the actual process of degeneration—occurs from the central end, and pushes from it to the periphery, being a repetition of the original process of nerve-development. The axis-cylinders of the central end hypertrophy, and if examined two or three months after section, are found to give off fine pale fibres from their club-shaped ends; these grow in length and breadth, insinuate themselves along the old track, develop a medullary sheath, and become new nerve-fibres. It remains to be stated that this process of degeneration and regeneration of nerve is to some extent a normal physiological phenomenon; the same nerve-fibres do not persist indefinitely during life, but some are dying while others are growing up; in a normal nerve, on careful examination, a few degenerating nerve-fibres are discover-

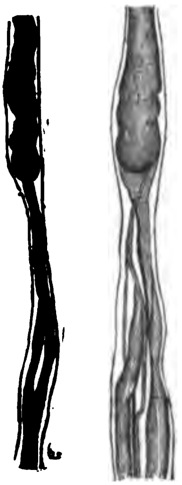
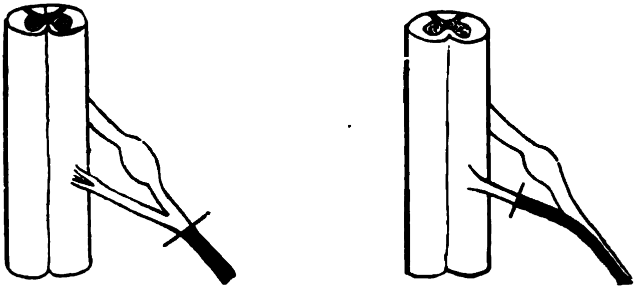


FIG. 148.—REGENERATING NERVE-FIBRES; MONTHS AFTER SECTION. (Ranvier.)

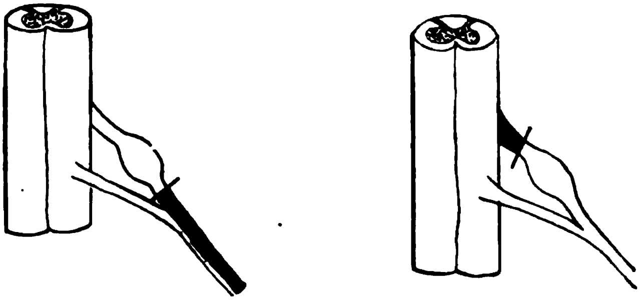
able, as well as numerous fine fibres, non-medullated as well as medullated, which not improbably include young fibres.

Primary union of nerve, with immediate restoration of conductibility, has never been experimentally realised, and the cases on record of return of sensibility or of motility in parts after accidental division of nerves, cannot be received as evidence to counterbalance the undoubted fact that any section, however carefully the cut ends are brought together, entails degeneration in the peripheral end, and loss of function, which require *months* to be recovered from. It is more probable in such cases that the nerve has been temporarily compressed, or that recurrent sensory fibres have recovered excitability after a temporary depression by 'shock.'



Degeneration of efferent and of afferent fibres below a section of entire nerve.

Degeneration of efferent fibres below a section of anterior root.



Degeneration of afferent fibres below a section of posterior root beyond the ganglion.

Degeneration of afferent fibres above a section of posterior root above the ganglion.

FIG. 149.—DIAGRAMS TO ILLUSTRATE WALLERIAN DEGENERATION OF NERVE-ROOTS.

It is the entire peripheral end of a mixed nerve that degenerates, *i.e.* motor and sensory nerves degenerate irrespectively of any direction of function in them. If the anterior root of a spinal nerve be divided, the degeneration is of the peripheral end. If the posterior root of a spinal nerve be divided *below the ganglion*, the degeneration is likewise of the *peripheral* end. But if the posterior root be divided above the ganglion, the degeneration is of the central end. From these facts it is concluded that the normal nutrition of motor nerve-fibres is dependent upon the grey matter of the spinal cord, while that of sensory nerve-fibres is dependent upon the ganglion of the posterior root.

The grey matter of the cord (*i.e.* the cells of the anterior cornua) and the ganglia of the posterior roots are spoken of in this capacity as the '*trophic*' centres of the fibres of the anterior and of the posterior roots respectively. These are fundamental facts; two supplementary points should however be mentioned. (1) After the anterior root has been divided, its peripheral end degenerates with the exception of a few fibres which remain normal in the peripheral end amid the mass of degenerated fibres, and the central end contains a few degenerated among the large majority of normal fibres; after the posterior root has been divided below the ganglion, a few degenerated fibres are discoverable in the anterior roots. These few exceptional fibres are the recurrent sensory fibres alluded to below (p. 475); they have their trophic centre in the ganglion of the posterior root. (2) According to Max Joseph there are also in the posterior root a few fibres which escape the general degeneration on their separation from the ganglion; the posterior root being cut, a few fibres are found degenerated in the peripheral end, a few fibres are found normal in the central end; these presumably are fibres which have their trophic centre in the cord and simply traverse the ganglia; similarly a few fibres are found degenerated in the posterior root above the section of the mixed nerve; these presumably have their trophic centre at the periphery.

Trophic Nerves.—There is abundant evidence to show that nerves can influence the nutrition of tissues, but whether they do so by a direct trophic action, or indirectly by causing vascular modifications, or otherwise, is the question we have now to examine. We have positive evidence that in the nervous system itself, nerve-cells exercise a trophic influence upon nerve-fibres, but this definite knowledge nowise includes or answers the question we are now putting, and which we may formulate as follows: Are nerves in general, or in any one indisputable case, the channels of an influence directly modifying the nutrition of peripheral tissues, independently of vascular or other changes? Is there any proof of the existence of 'trophic' as distinguished from 'motor,' 'secretory,' or 'inhibitory' nerves?

The cases in point which naturally come first to mind are (1) the effects of division of the fifth nerve, and of the superior laryngeal nerve; (2) the effects of division of the cervical sympathetic, and of other nerves in young, rapidly-growing animals; (3) clinical incidents, especially the appearance of 'bed-sores' and of 'glossy skin' on paralysed parts, and of herpes along the course of intercostal nerves.

The last-named items, however interesting in themselves, are in reality not admissible in either an affirmative or a contradictory sense as regards the answer to the questions stated above. No doubt the nutrition of paralysed parts is altered, and bed-sores develop with surprising rapidity; equally surely in the case of herpes a trophic disturbance runs along the course of nerves; but we have no proof that the malnutrition is a direct trophic effect, to the exclusion of the unnoticed rough usage or prolonged pressure to which anæsthetic parts are liable, or—in the case of herpes—to the exclusion of vaso-motor changes.

Turning next to experimental data, we have also to dismiss as imperfect evidence the greater growth of a young rabbit's ear after section of the cervical sympathetic, the greater growth of the maxillary bones after section of the facial nerve, and the wasting of an inferior extremity after section of the sciatic nerve; the first two instances are obviously attributable to increased vascularity of the parts, the third is the extremely gradual effect of paralytic disuse of the limb, or an acute effect of which the intimate mechanism is most obscure; an acute muscular atrophy of such character with 'reaction of degeneration' (see p. 365) is perhaps the nearest approach we possess to *evidence* of the existence of trophic nerves, but it is not '*clean*' evidence. We cannot say whether the effects are paralytic or irritative, nor whether they are direct or indirect or vascular, and there are discrepancies between the clinical and the experimental phenomena upon which we cannot enter here, but which must be cleared away before the evidence can be admitted as unequivocal.

The next case we have to consider is that of the fifth nerve, to which, more than to any other nerve, appeal has been made by experiments in this connection. Shortly, the facts are these. After section of the fifth nerve the eye becomes inflamed, the cornea ulcerates, the entire eyeball suppurates and is lost. To the conclusion that these are an instance of trophic disturbance, objection has been raised to the following effect:—After section of the nerve, the conjunctiva and the cornea lose sensibility, foreign bodies lodge themselves unnoticed on the eyeball, and give rise to inflammation. In support of this interpretation it has been shown that, by careful protection of the eye, its disorganisation can be—if not entirely prevented—at least considerably postponed. In sum, when we consider how difficult it must be to permanently and perfectly protect the eyeball of an animal from external irritation, and moreover that even then we have not excluded the possible participation of a vascular factor, we are driven to admit that the direct trophic action of nerve, tried by the test case of the fifth nerve, remains unproven. And in questions of this nature, until an action has been proved to exist, it does not exist, however probable it may appear. The last case we have to consider is that of the superior laryngeal nerve as regards its trophic influence upon the laryngeal muscles. Exner has recently discovered upon the horse that these muscles undergo acute atrophy after section of the nerve, in marked contrast with the chronic atrophy consequent upon section of the inferior laryngeal nerve; the great significance of this case lies in the fact that an alteration of nutrition takes place in a *motor* organ after section of a sensory nerve; and if we have not included this item in the main argument of the question, it is only because the observations have not yet been matured by the criticism of independent observers; but even accepting them as fully established, the further question remains open whether the effect is an illustration of direct trophic action, or of the necessity of centripetal influences as a factor in normal nutrition.

Stimuli.—Any cause which provokes a nerve to action is called a *stimulus*. The evidence that a nerve has been stimulated is in the immense majority of cases a *movement* of some kind; each individual 'ego' may, however, experience for himself another evidence of nerve-stimulation in the form of a *sensation*, without manifesting the fact by any external movement. The evidence of *sensation* in other persons or in animals is furnished by the movements whereby their feelings are or appear to be expressed. Such evidence is indirect; the observer hears statements, or sees and interprets the significance of muscular expressions; these are, of course, movements or attitudes; obviously the value of such evidence varies greatly with the aptitude and training of the observer. A third kind of evidence is available in the laboratory on exposed nerves; the electrical state of nerve is altered when it is rendered active; and the alteration (negative variation or current of action) is demonstrable by the galvanometer, or by the electrometer (pp. 308, 314). Movement as evidence of the passage of motor impulses, the negative variation as evidence of the passage of centripetal or centrifugal impulses, are objective signs. Sensation, as evidence of the passage of sensory impulses, is a '*subjective*' sign. Movement, as evidence of the passage of sensory impulses, is a mixed sign—*i.e.* a movement is seen, and *inferred* to be an expression of sensation. Objective signs are less liable to fallacy than subjective or mixed signs. Hence, as a rule, it is easier to ascertain loss of motion than loss of sensation.

Nerve in common with all protoplasm possesses excitability, and the salient characteristic of this excitability in the case of nerve is its transmission along the fibre; hence it is termed *conductibility.* The transmission is not, as in the case of circulation, any actual transmission of matter, but only the transmission of a state of matter from particle to particle. The direct local excitability of nerve to artificial stimuli, applied at any point of its course, is sometimes distinguished from its indirect excitability to the impulse starting from that point and transmitted onwards. The distinction has its justification in experimental and in clinical facts, for it sometimes happens that the local excitability to a direct stimulus is lost at a part of the nerve which can still be traversed by impulses transmitted from above. This is apt to occur clinically during the progress of recovery from paralysis, owing to previous lesion or disease of motor nerve; it has been observed that muscles may be voluntarily set in action through motor nerves which have not yet recovered their electrical excitability. The converse may be experimentally demonstrated, viz. a nerve may be rendered impermeable while still remaining directly excitable.

Stimuli may be natural or artificial. Natural stimuli may arise in the brain or at the periphery, and their consequent impulses may pass from the brain to the periphery, or from the periphery to the brain. All appreciable qualities of objects in the surrounding world are natural stimuli at the sensory periphery, all consequent volitional impulses and ideas of intended movements are natural stimuli at the supreme motor centre. The natural stimuli at the sensory periphery are the physical qualities of objects which excite *smell, sight, hearing, taste, touch,* and possibly '*muscular sense,*' '*thermic sense,*' and '*pathic sense.*' To these qualities we give the names smell, light, sound, taste, smoothness or roughness, resistance and extension, weight, heat, cold, pain. Some of these stimuli affect us best when we meet them half-way by some action of our own, by a state of voluntary attention, or by actual movements. An object is best seen when it is looked for, a sound best heard when it is listened for. We generally sniff to smell, and move in our mouths substances which are to be tasted, and movement on our part is necessary for anything like delicate appreciation of the nature of a surface, or the weight and size of an unseen object.

Artificial stimuli are such as are applied experimentally. They may be *mechanical, chemical, thermic,* or *electrical,* and the latter may be in the form of *induced, constant,* or *static* electricity. Of these various kinds of stimuli the electrical, in the form of *induced currents,* is that of most frequent and convenient experimental application. The effects of the constant current have also been exhaustively studied. Those of static electricity are only incidentally observed, this form being rarely employed in the laboratory; '*unipolar stimulation*' (*i.e.* only one pole being applied to the nerve) is due to a discharge of static electricity, and is demonstrated as a fallacy to be guarded against in experiments.

Mechanical stimulation.—A sudden smart blow upon a motor nerve causes muscular contraction; a blow upon a sensory nerve causes pain. This is easily experienced on the ulnar nerve, which is a mixed nerve composed of sensory and of motor fibres. When it is struck just where it lies upon the bone, there result the sensation of tingling or pain, and a twitch of the muscles which are served by the nerve. In the laboratory, mechanical stimulation is applied by means of Heidenhain's tetanomotor—or of an instrument devised for the same purpose by Tigerstedt. This form of stimulation supplies the best available means for the demonstration of electrotonic alterations of excitability in the intrapolar region of a nerve during the passage of the constant current.

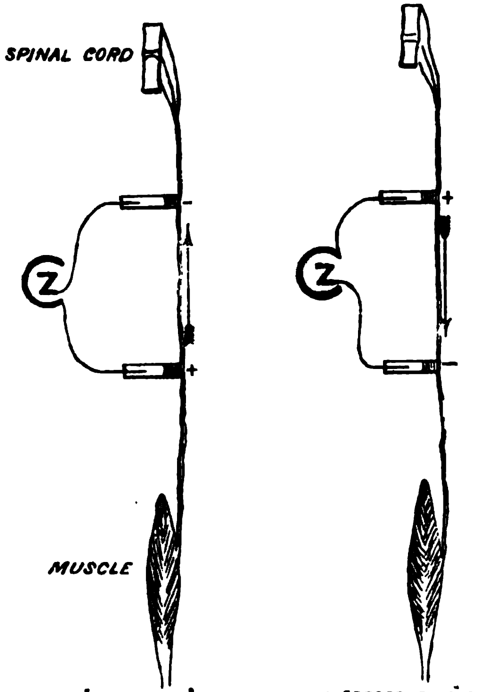
Of *thermic* stimuli there is little to be said; if heat be applied *suddenly* it may act as a stimulus, also upon a change from a medium or low to one of high temperature, nerves are prone to fall into a *tetanic* state, the muscles which they supply becoming contracted, and so remaining for long periods. The action of *chemical* stimuli has been carefully studied, but at the time when this was done an important source of fallacy was not recognised, and the results which were obtained must therefore be regarded as inconclusive. The method followed was to allow the cleanly cut end of the nerve of a nerve-muscle preparation to touch a minute drop of a solution of the substances under investigation.

Effects of the constant current.—These are studied upon *nerve-muscle preparations.* The nerve is laid across two *unpolarisable* electrodes through which it receives the current from a battery. The effects to be studied are, (1) those which take place when the current commences and ceases to flow through the nerve, *i.e.* at *make* and at *break*; (2) *electrotonic currents,* which spread along the nerve on either side of the two electrodes; (3) *alterations of excitability* which accompany these electrotonic currents.

Make and break effects.—Pflüger's law.—When the current is *made* or when it is *broken,* or at both these events, there is contraction of the muscle, which is evidence that the nerve has been stimulated. In other words, the constant current stimulates the nerve when it *commences* and when it *ceases* to pass, but does not stimulate the nerve *while it is passing.* If now attention be given to the *strength* of current and to its *direction,* it is found that the contractions at *make* and at *break* of the current appear or fail to appear in a regular order. This is called Pflüger's law of contractions.

The terms *ascending* and *descending* are those in common use, and signify direction of current in the nerve in relation to nerve centre. Current is 'ascending' when its direction in the nerve is from muscle towards centre, 'descending' when its direction in the nerve is from centre towards muscle. But it simplifies matters to attend particularly to the points where the current *enters and leaves* the nerve; the point where the current enters is the *anode* (+), the point where the current leaves is the *kathode* (—).

The explanation of the above 'law' or formula is as follows. As stated below, when a current commences to flow, *i.e.* at *make* of a current, excitability of the nerve is *diminished* at and near the *anode, increased* at and near the *kathode.* A sudden increase of excitability is equivalent to a stimulus; therefore *at make of a current the stimulus is at the kathode.* As stated in the next paragraph, when a current ceases to flow, *i.e.* at *break* of the current, excitability at and near the anode suddenly recovers up to and beyond its normal level, while at and near the kathode it suddenly falls down to and beyond its normal. A sudden change of excitability from below normal to such normal, or above it, is equivalent to a sudden increase of excitability and furnishes a stimulus; therefore *at break of a current the stimulus is at the anode.*



AN 'ASCENDING' CURRENT A 'DESCENDING' CURRENT

FIG. 150.

With a current of 'medium' strength there is contraction at make and break of ascending and of descending currents, contractions at make being excited from the kathode (—), contractions at break being excited from the anode (+), and the formula reads,

$$\overset{\text{ASC.}}{\overset{m.}{\text{C.}}\quad\overset{b.}{\text{C.}}}\quad\overset{\text{DESC.}}{\overset{m.}{\text{C.}}\quad\overset{b.}{\text{C.}}}$$

With a 'weak' current only the more efficient stimulus is effective. The sudden increase at the kathode when the current is made is more effectual than the sudden release at the anode when the current is broken. Hence with a weak current contractions appear at make only with either direction of current, and the formula reads,

$$\begin{array}{cccc} \multicolumn{2}{c}{\text{ASC.}} & \multicolumn{2}{c}{\text{DESC.}} \\ m. & b. & m. & b. \\ \text{C.} & \text{O.} & \text{C.} & \text{O.} \end{array}$$

With a 'strong' ascending current the point of stimulation at make is the kathode, but between it and the muscle lies the anode at which excitability is diminished. With such a strong current the diminution is sufficient to block the passage of the stimulus from the kathode. Hence the make contraction fails to appear.

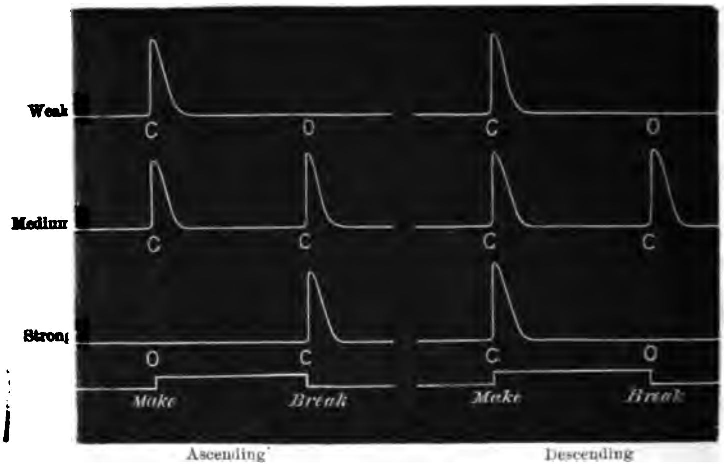


FIG. 151.—PFLÜGER'S LAW OF CONTRACTIONS ON NERVE-MUSCLE PREPARATIONS.

At break, the stimulus at the anode, having no obstacle between it and the muscle, produces a contraction. With a strong descending current the anode does not separate the kathode from the muscle, and the make stimulus at the kathode produces a contraction. At break, however, the stimulus is produced at the anode, between which and the muscle there intervenes the kathode where excitability suddenly diminishes; this diminution is sufficient to block the stimulus from the anode, and the formula reads,

$$\begin{array}{cccc} \multicolumn{2}{c}{\text{ASC.}} & \multicolumn{2}{c}{\text{DESC.}} \\ m. & b. & m. & b. \\ \text{O.} & \text{C.} & \text{C.} & \text{O.} \end{array}$$

Ritter's tetanus.—It frequently happens that at break of the galvanic current, the muscle enters into tetanus; this is due to an after-anodic excitation, and the effect is also demonstrable by the galvanometer ('positive polarisation current,' p. 368.)

The formula of contraction on man.—The above statements are based upon experiments with the nerves of frogs; experiments on man give results of which the principle is the same, but with differences which are owing to differences in the conditions of experiment. In the case of a frog's nerve cut out of the body, the points of entrance and of exit of the current by which it is traversed are usually chosen some distance apart, so that the kathode and anode are distinct, the current entering the nerve at one electrode and leaving it at the other. In the case of human nerve the conditions are different, for the nerve is imbedded in the tissues below the skin. A pair of electrodes cannot be applied to a nerve so as to send a current in at one point, out at another point; so that it is incorrect to speak of 'ascending' and 'descending' currents under such circumstances, and it is useless to attempt to study the effects when both electrodes are applied along the course of one and the same nerve. We must apply one electrode only to the nerve, and attend to its effects alone, completing the circuit through a second electrode which is applied according to convenience to some other part of the body. Confining our attention to the first electrode, let us see what will happen according as it is *anode* or *kathode* of a galvanic current. If this electrode be the anode of a current, the latter enters the nerve by a series of points, and leaves it by a second series of points; the former or proximal series of points collectively constitutes the *polar* zone or region, the latter or distal series of points collectively constitutes the *peripolar* zone or region. In such case the polar region is the seat of entrance of current into the nerve, *i.e.* is *anodic*; the peripolar region is the seat of exit of current from the nerve, *i.e.* is *kathodic*. If on the contrary the electrode under observation be the kathode of a current, the latter enters the nerve by a series of points which collectively constitute a 'peripolar' region, and it leaves the nerve by a series of points which collectively constitute a 'polar' region. The current at its entrance into the body diffuses widely, and at its exit it concentrates; its 'density' is greatest close to the electrode, and the greater the distance of any point from the electrode the less the current density at that point; hence it is obvious that the current density is greater in the polar than in the peripolar region.

These conditions having been recognised, we may apply to them the principles learned by study of frogs' nerve under simpler conditions. Seeing that with either pole of the battery, whether anode or kathode, the nerve has in each case points of entrance (constituting a collective anode), and points of exit to the current (constituting a collective kathode); and admitting as proved that make excitation is kathodic, break excitation anodic, we may with a sufficiently strong current expect to obtain a contraction at make and at break with either anode or kathode applied to the nerve. And we do so in fact. When the kathode is applied, and the current is made and broken, we obtain a *kathodic make contraction* and a *kathodic break contraction*; when the anode is applied, and the current is made and broken, we obtain an *anodic make contraction* and an *anodic break contraction*. These four contractions are, however, of very different strengths; the kathodic make contraction is by far the strongest; the kathodic break contraction is by far the weakest; the kathodic make contraction is stronger than the anodic make contraction; the anodic break contraction is stronger than the kathodic break contraction. Or otherwise regarded, if instead of comparing the contractions obtained with a 'sufficiently strong' current, we observe the order of their appearance with currents gradually increased from weak to strong, we shall find that the kathodic make contraction appears first, that the kathodic break contraction appears last, and the formula of contraction for man reads as follows:—

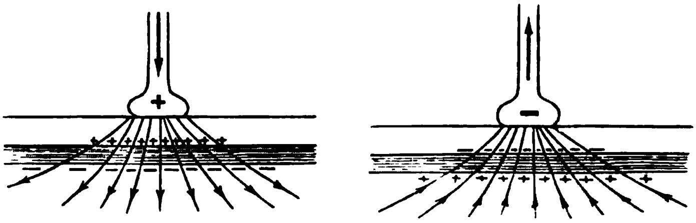


Fig. 152.

Anode of Battery.
Polar region of nerve is anodic.
Peripolar region of nerve is kathodic.

Kathode of Battery.
Polar region of nerve is kathodic.
Peripolar region of nerve is anodic.

Weak current . . .	K.C.C.	—	—	—
Medium current . .	K.C.C.	A.C.C.	A.O.C.	—
Strong current . .	K.C.C.	A.C.C.	A.O.C.	K.O.C.[1]

[1] K.C.C. = Kathodic closure contraction.
A.C.C. = Anodic closure contraction.
A.O.C. = Anodic opening contraction.
K.O.C. = Kathodic opening contraction.

That such should be the normal order of appearance is fully accounted for by the following considerations:—

In the	The nature of the stimulus is	The situation of stimulus is	
K.C.C.	Kathodic	Polar	= best stimulus in best region
A.C.C.	Kathodic	Peripolar	= best stimulus in worst region
A.O.C.	Anodic	Polar	= worst stimulus in best region
K.O.C.	Anodic	Peripolar	= worst stimulus in worst region

which also account for an apparent anomaly, viz. that sometimes the anodic closure contraction precedes the anodic opening contraction, while sometimes this order is reversed; this difference depends upon relative current densities in the two regions, which are determined by the nature of the tissues by which the nerve is surrounded. This point need not, however, be further discussed here.

The latent period of the break contraction on man is exceedingly and constantly long (·05″); on the frog its duration is very variable, sometimes very short, sometimes very long. With strong currents, it is usual on man to obtain tonic contraction during the passage of the current—*galvanotonus*—as well as single twitches at make and at break.

The reaction of degeneration is a term used to denote the reaction of diseased nerve and muscle on man. As regards *nerve*, the reaction of degeneration consists in an abolition of excitability to the constant current and to the induced current. As regards *muscle*, the reaction of degeneration consists in the abolition of excitability to the induced current, while the excitability to the constant current is exaggerated; the muscular contraction is also greatly prolonged, and galvanotonus is easily produced. The normal contraction-formula given above is departed from, the most characteristic feature of this departure being a reversal of the normal order of appearance of K.C.C. and A.C.C.; normally K.C.C. appears with a weaker current than A.C.C., in a well-marked reaction of degeneration A.C.C. appears with a weaker current than K.C.C. There is no satisfactory explanation to be given of this reversal.

According to recent observations by Gotch, variations of temperature alter the relative efficacy of long and of short stimuli applied to frog's nerve, long stimuli being favoured by low, short stimuli by high temperature.

Electrotonus.—The term electrotonus is used to denote two distinct series of effects which are produced when the constant current is applied to a nerve. The effects are (1) electrical currents in the nerve beyond the part of it which is traversed by the experimental current; these currents are known as the '*electrotonic currents*,' and the phenomenon is called '*electrotonus*;' (2) alterations of the excitability of the nerve in and near the part which is traversed by the current; this phenomenon is intimately associated with the electrotonus just mentioned, and is itself commonly called 'electrotonus;' but, seeing that these are alterations which accompany electrotonus, it is better to distinguish them by the longer expression, *electrotonic alteration of excitability*. Electrotonic currents and electrotonic alterations of excitability are to be studied with reference to the poles at and near which they are produced, and may be in either of two opposite directions. An electrotonic current in the vicinity of the anode is called '*anelectrotonic*,' an electrotonic current in the vicinity of the kathode is called '*katelectrotonic*.' The corresponding alterations of excitability which are found are likewise called 'anelectrotonic' and 'katelectrotonic,' according as they occur in the vicinity of the anode or of the kathode. The terms 'anelectrotonus' and 'katelectrotonus' are frequently used indiscriminately to denote the currents or the alterations of excitability. It is obviously advisable to use the terms electrotonic, katelectrotonic, and anelectrotonic currents, or electrotonic, katelectrotonic and anelectrotonic alterations of excitability, in preference to the terms electrotonus, katelectrotonus, and anelectrotonus, seeing that these last have double meanings.

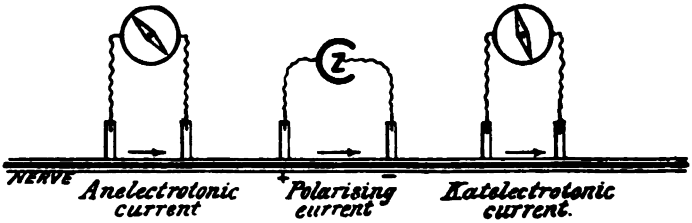


FIG. 153.

Electrotonic currents.—If through one pair of unpolarisable electrodes a constant current be passed into a portion of nerve, while a second pair of electrodes 'lead off' from some other portion of the nerve to a galvanometer, the galvanometer will indicate a current derived from the second pair of electrodes. This is the electrotonic current. The galvanometer will show that this current varies in direction according as the second pair of electrodes is situated near the anode, or near the kathode of the experimental or '*polarising*' current. This direction will be in accordance with the arrows of the diagram; *i.e.* the electrotonic current in the nerve has always the same direction as that of the polarising current.

The electrotonic current caused in the vicinity of the kathode is called katelectrotonic, and is in the nerve directed *from* the region through which the polarising current is passing; that caused in the vicinity of the anode is called anelectrotonic, and is in the nerve directed *towards* the polarised region.

Electrotonic currents vary with the *intensity of the polarising current*, and with the distance of the 'led off' or electrotonic region from the polarised region of the nerve. With increasing intensity of the polarising current the consequent electrotonic current increases, and the increase is not limited, *i.e.* does not reach any maximum. With increasing distance of the 'led off' from the polarised region the electrotonic current is weaker. These characters contrast with those of the 'current of action,' which, when it appears, quickly reaches a maximum, and does not diminish in strength with increasing distance of the 'led off' region from that through which the experimental current is passed. A third point of difference is that the electrotonic current bears no relation to the current of injury, and appears when any two points on the longitudinal surface are led off, while the current of action on nerve is generally manifested as the negative variation of an injury current, and is greatest when the latter is greatest. These characters distinguish the electrotonic current from the true action current, and show that it is not significant of an excitatory state of the living tissue. Is it, however, a purely physical phenomenon that can occur with any simple conductor? That it is not is indicated by the facts; 1. that it is abolished by a *ligature* between the polarised and the electrotonic regions; 2. that it is absent, or at least diminished on *dead* and on *degenerated* nerve; 3. that it is absent from tendon or a wet thread. These facts show that it is, if not dependent upon the *vital* integrity of nerve, at least closely associated with its *anatomical* integrity.

Cæteris paribus, the anelectrotonic is stronger than the katelectrotonic current. Both currents are increased by increasing the length of the polarising region, provided the current in that region, which is diminished by the increased resistance, is brought up to its original value by increasing the electromotive force.

Electrotonic currents can be reproduced on a model composed of a core of platinum wire, and a sheath of $ZnSo_4$ solution, between the contiguous surfaces of which polarisation gives rise to a virtual resistance, and consequent longitudinal diffusion of current in extrapolar regions. They may be provoked by induced as well as by constant currents, and this possibility must be specially borne in mind when induced currents are used for the study of the true negative variation or action current (*v.* p. 383).

The after-electrotonic currents obtained when the polarising current is cut off, are as follows:—in the intrapolar region the after-current is in the opposite direction, unless the polarising current has been 'strong' and of short duration, when an after-current in the same direction is obtained (du Bois-Reymond's 'positive' polarisation current). In the extrapolar region the after-current on the side of the kathode is in the same direction as the katelectrotonic current; the current on the side of the anode is at first in the same, subsequently in an opposite direction, to that of the anelectrotonic current.

Du Bois-Reymond's positive polarisation current is demonstrable on nerve and on muscle. Strong currents of short duration are favourable to its manifestation, and the nerve or muscle must be alive. With weaker currents of longer duration, ordinary polarisation currents, negative to the original current, are obtained, and these effects are obtainable on dead as well as on living muscle or nerve. Hermann has shown that the 'positive' polarisation current is in reality an action current arising from an after-anodic excitation.

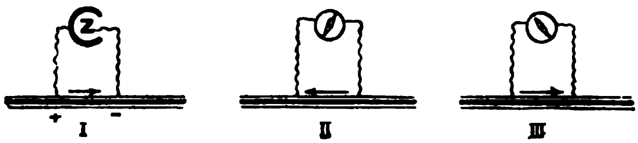


FIG. 154.—INTRAPOLAR AFTER-CURRENTS.

I. Original, or polarising current.
II. Ordinary polarisation after-current (negative).
III. 'Positive' polarisation after-current.

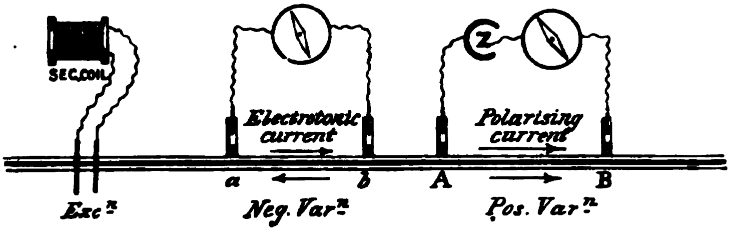
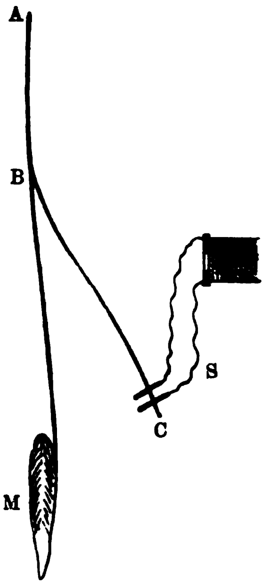


FIG. 155.

The polarising current passes in the nerve from A to B. An electrotonic current passes in the nerve in the direction *a* to *b*. During excitation the polarising current is increased, the electrotonic current is diminished.

Negative variation of electrotonic currents. Positive variation of polarising currents, or polarisation increment.—If a nerve through a portion of which a polarising current is passing, giving rise to electrotonic currents in the remainder of the nerve, be excited by faradisation, the strength of the polarising and of the electrotonic currents will be altered; the strength of the polarising current will be increased, that of an electrotonic current will be diminished. The former effect is usually spoken of as the polarisation increment, the latter is known as the negative variation of the electrotonic current. They are in reality action currents.

The paradoxical contraction.—If the branch B C of a *divided* nerve be stimulated at S by an induced or constant current, the muscle M contracts. This is not a reflex contraction, seeing that the nerve is separated from the spinal cord. It is due to an electrotonic current spreading along the fibres of B C beyond the point of junction B, and exciting in the joint portion A B adjacent fibres which are distributed to the muscle M.



Paradoxical Contraction

FIG. 156.

Electrotonic alterations of excitability.—If, while a polarising current is passed through a portion of nerve in the manner above described, the excitability be tested at various parts of the nerve, differences will be found—namely, an *increase* of excitability near the *kathode*, a *diminution* of excitability near the *anode*. Or otherwise, if, while tetanising currents are being passed through a nerve, a polarising current is passed through the nerve for a given period, it is found that the effect of the tetanising current is modified during that period—*increased* if the polarising *kathode* be near the point of application of the tetanising current, *diminished* if the polarising *anode* be near the point of application of the tetanising current, and is less and less further and further from the anode; similarly, the increase of excitability is greatest close to the kathode, and is less and less further from the kathode. This is expressed in the following diagram (fig. 159).

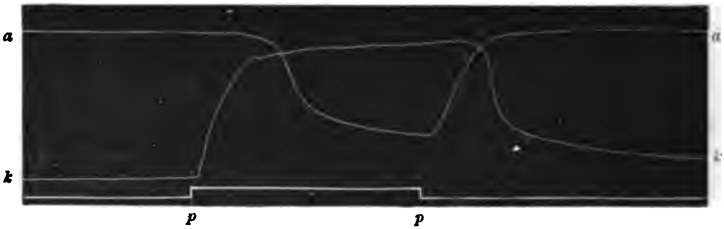


FIG. 157.—ELECTROTONIC ALTERATIONS OF EXCITABILITY. NERVE-MUSCLE PREPARATION.

Insufficient tetanising stimuli produce a tetanus (line *k k*) during the passage of a polarising current with the kathode near the exciting electrodes. A tetanus (line *a a*) is cut down during the passage of a polarising current during the period *p p* with the anode near the exciting electrodes.

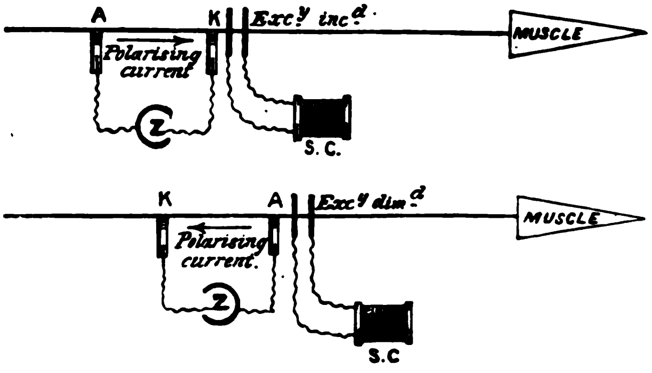


FIG. 158.

Diminished excitability near the anode is called 'anelectrotonic,' increased excitability near the kathode is called 'katelectrotonic,' or shortly, anelectrotonus and katelectrotonus; but these terms, as above explained, are ambiguous.

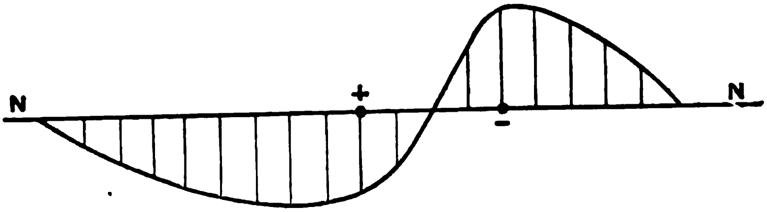


FIG. 159.

N N is a line to denote a nerve and at the same time the level of normal excitability, *i.e.* that observed in the absence of any polarising current; + and − denote respectively the anode and kathode of a polarising current; the region included between them is the intrapolar region. The degree of altered excitability at various points of the nerve near the anode and kathode respectively is indicated by perpendicular lines below and above the normal N N. A line joining their summits indicates the mode of distribution of the altered excitability at and near the anode and kathode of the polarising current. The excitability of the anode is most diminished at the anode, less diminished in its immediate vicinity, still less diminished at more remote points. The excitability of the kathode is most increased at the kathode, less increased in its immediate vicinity, still less increased at more remote points. (Pflüger.)

Experiments on man.—The above conclusions are based upon experiments made upon frogs' nerves. Experiments on man give similar results with minor differences, owing to differences in the conditions of experiments. As regards frogs' nerve, it is isolated, and the test is applied separately from the polarising current, induction currents being most convenient for testing the extrapolar region, while mechanical stimuli are best adapted for testing the intrapolar region. As regards human nerve imbedded in the tissues, such a mode of testing is not possible, and it is necessary to adopt some means for ensuring that the test shall coincide with the polarised region of the nerve. This can be effected by conjoining in one circuit the testing with the polarising current, or in the case of mechanical stimuli by applying the latter through the electrode of the polarising current.

The effect of an induction shock alone, is compared with its effect in the presence of a polarising current; the difference observed is owing to the modification of excitability which the polarising current produces. The polar effects under the conditions of application of electricity to the human body, and the distinction between polar and peripolar excitation (p. 364), must be borne in mind in this connection. Remembering that a current entering or leaving the body through an electrode applied over a nerve, has in that nerve a polar and a peripolar region—polar of the same sign as the electrode, peripolar of the opposite sign; remembering further that make excitation is kathodic, break excitation anodic, it is easy to understand the effects of various possible combinations between testing and polarising currents. If the induction current is used as the test, the combinations which it is possible to form at the exploratory electrode with a polarising current in the same circuit, are as follows:—

1. Kathode of testing current, and of polarising current.
2. Anode of testing current, and of polarising current.
3. Kathode of testing current, and anode of polarising current.
4. Anode of testing current, and kathode of polarising current.

Putting these four cases to the test, it will be found that excitability is *increased* in the polar region when it is *kathodic*, *diminished* when it is *anodic*, and that similarly, but in smaller degree, excitability is increased in a peripolar kathodic region, diminished in a peripolar anodic region.

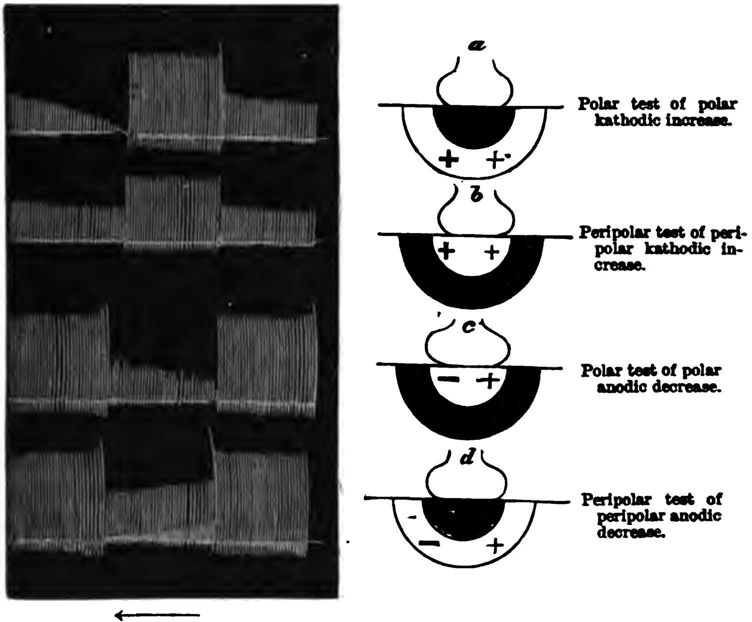

a
+ +
Polar test of polar kathodic increase.
b
+ +
Peripolar test of peripolar kathodic increase.
c
− +
Polar test of polar anodic decrease.
d
− − +
Peripolar test of peripolar anodic decrease.
After
←
During polarisation.
Before

FIG. 160.

Similar results follow the application of other tests—make and break of a constant current alone, and in the presence of a polarising current in the same circuit—mechanical stimulation alone and during the passage of a polarising current—viz. increased excitability in a kathodic region, diminished excitability in an anodic region.

Sensory nerves.—The statement applies to motor and sensory nerves alike. On the former it may be demonstrated by the graphic method, on the latter it requires to be experienced in the form of sensation by the observer himself becoming the subject of experiment. Experiments on man present the advantage that alterations of sensory excitation can be better appreciated by the subjective evidence of sensibility, than by the objective signs from which inferences are drawn in the case of animals.

After-effects.—Not only does the constant current cause a modification of excitability during its passage, but it leaves excitability altered after it has ceased to pass. The ultimate after-effect is always an increase of excitability, but in the case of the kathodic after-effect the increase is preceded by a brief period of diminished excitability.

Rapidity of transmission of nervous impulses.—The rate at which an impulse travels along a nerve can best be determined for *motor transmission* along an ordinary mixed nerve. The experiment is as follows:—

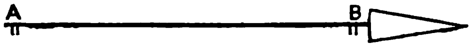


Fig. 161.

An induction shock is sent into the nerve at B as close as possible to the muscle, and the interval between the application of the stimulus and the commencement of the resulting contraction is recorded. A second induction shock is sent into the nerve at A as far as possible from the muscle; the interval between stimulus and contraction is measured as before. This second interval is longer than the first by a fraction of a second, and the difference is owing to the time which the stimulus at A requires for its passage from A to B. Given this difference of time and the distance between A and B, it is easy to calculate the rapidity per second. Thus, if the difference is $\frac{1}{100}$ sec., and the distance $\frac{1}{2}$ meter, the rapidity is 50 meters per second. This is about the rapidity of motor transmission in *human nerve,* as may easily be determined by recording a pair of contractions of the flexor muscles of the fingers—the one contraction caused by an induction shock to the cervico-brachial plexus above the clavicle, and a second contraction by an induction-shock to the median nerve at the bend of the elbow.

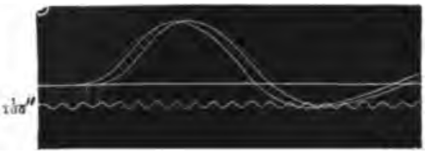


FIG. 162.—VELOCITY OF MOTOR IMPULSE IN HUMAN NERVE.

The experiment was first made *on the frog* by Helmholtz, just after it had been proclaimed by Johannes Müller that the rapidity with which nervous impulses travel must remain concealed from us. Helmholtz found that at ordinary temperature the rapidity is about 30 meters per second, and he soon afterwards made measurements on man with the same result, viz. a rapidity of 30 meters. Small animals are obviously less adapted to such determinations than large; the rapidity is not markedly lower on cold-blooded animals at ordinary temperature, but is greatly diminished at low temperatures. On the frog, for instance, it is found to be only 1 meter per second at 0°.

The rate of transmission of the electrical disturbance (*negative variation* or current of action, see p. 383), which accompanies the nerve-impulse, has been measured by Bernstein with the same result, viz. a rapidity of about 30 meters per second.

Attempts have been made to determine the rapidity of transmission of impulses *along sensory nerves*, and it is stated to be the same as that along motor nerves. The method followed has been to stimulate at points of nerve near and far from a centre, and to record the interval between each stimulus, and the consequent reflex contraction. The difference is attributed to time occupied in the passage of a centripetal impulse along the afferent channels. Obviously, however, the data towards this conclusion are less cogent than in the case for motor transmission, for the impulse has to pass a nerve-centre, and the delay which it there undergoes is not only great but *variable*. The data which are obtained by stimulating at points of the skin near and far from the cerebro-spinal axis (*e.g.* at the shoulder and at the fingers, or at the thigh and at the foot), and comparing the reaction times of voluntary response to such stimuli—are still less satisfactory for the purpose of estimating rate of transmission in sensory nerves. The variants in such reaction times are too great, both as regards central delay and cutaneous sensibility, to permit of exact data being obtained.

The only exact method of measuring the rate of a sensory impulse would be to measure the rate of propagation of the negative variation along a pure afferent nerve. This has not been done, and would indeed be almost superfluous, for we may legitimately accept in its stead the rate of transmission of the negative variation in mixed nerves as an index of the speed at which an impulse travels along all medullated fibres in either direction.

It is probable that the rate of transmission is lower in non-medullated than in medullated fibres; but there are no exact data in point.

Conduction in both directions.—Afferent nerves normally conduct impulses in one direction only—from periphery to centre. Efferent nerves normally conduct impulses in one direction only—from centre to periphery. And when an afferent or an efferent nerve is stimulated at some point of its course, the effect is manifested in the former case at a sensory centre, in the latter case at the motor periphery. There is however evidence to show that nerves of either kind are capable of transmitting impulses in both directions, though in one of these directions in each case no effect is manifest. If a pure motor nerve is stimulated at the point B, the muscle contracts, and gives evidence that a nervous impulse generated at B has passed from B to C. It does however also pass from B to A, but to prove this requires a special test, for the motor nerve does not possess any means at the centre of revealing the fact. The electrical disturbance or 'current of action,' which accompanies any action in nerve, furnishes this proof—when B is stimulated, it is demonstrable between B and A as well as between B and C, *i.e.* it is transmitted in both directions. Similar proof has been given of the passage of impulses in both directions along afferent nerves.

FIG. 163.

A second proof as regards afferent nerves is afforded by an experiment of Paul Bert. He grafted the tip of one rat's tail to the nose of another rat, and when union had been effected amputated the tail near its base. The second rat was thus provided with a trunk-like appendage, and after a time obtained sensory connection with the artificial organ, and gave evidence of sensation if it were pinched. Under these circumstances the impulse passed from base to tip of the tail, whereas formerly it passed from tip to base.

Kühne's gracilis experiment proves the point on an efferent nerve. The gracilis muscle of the frog is in two portions with a tendinous intersection, and supplied by a nerve which divides into two chief bundles; excitation strictly limited to *one* of these bundles causes *both* portions of the muscle to contract.

Inequalities of excitability.—A nerve is not equally excitable at all points of its course, nor in all the fibres of which it is composed. Instances in point are, (1) the comparative excitability of the motor nerve-fibres distributed to extensor muscles of a limb, and of those distributed to the flexor muscles, and (2) the comparative excitability of the vaso-dilatator and vaso-constrictor fibres contained in a mixed nerve. If the sciatic nerve be stimulated in the frog with tetanising currents of gradually increasing strength, the limb will at first become flexed, and, as the current strength increases, the flexion will give place to extension. This is considered to show that the nerve-fibres to flexor muscles are excitable by weaker stimuli—(*i.e.* are more excitable)—than the nerve-fibres to extensor muscles. Analogous observations have been recorded, relating to the excitation of vasomotor nerves, and the usual result of primary vaso-constriction followed by secondary vaso-dilatation—also the facts, that with weak currents vaso-constrictor action is better manifested, while with strong currents vaso-dilatator action is more prominent, have been explained as being due to greater excitability of vaso-constrictor in comparison with vaso-dilatator fibres. But the experimental data are not very precise, nor very easily obtained.

Unequal excitability at different points along the course of a nerve can only be observed on excised nerve (for apparent inequalities in nerves imbedded in the tissues need not at all be inequalities of excitability—they are due to inequalities of excitation according as the nerve is more or less accessible to the application of currents), and was for long an unexplained phenomenon. But it is now understood to be owing to local injury, of the trunk itself, or of the large branches which must be cut through when the nerve is excised, and it is found that when a nerve is excised with the greatest care, the maxima of excitability correspond with the points where large branches come off from the trunk of the nerve.

A notable theory, known as *the avalanche theory*, was advanced by Pflüger; it was to the effect that a stimulus gathers strength in its passage down a motor nerve, so that a weak stimulus of the nerve far from the muscle would produce a greater effect than a similar stimulus nearer to the muscle. But the fact and the theory have been entirely discredited by subsequent observers, and it is now accepted that the nervous impulse neither gains nor loses in strength in its passage, but remains throughout of uniform strength.

Ritter-Valli 'law.'—The Ritter-Valli 'law,' so-called, is a simple assertion of fact, and an additional example of unequal excitability at various points along the course of a nerve. The nerve of a nerve-muscle preparation is immediately after excision more excitable at its upper portion near the cut end than at its lower portion near the muscle. With the lapse of time it is found that the increased excitability of the upper as compared with the lower end gives place to diminished excitability, which gradually falls to zerò, and this loss of excitability progresses in a centrifugal manner along the nerve towards the muscle, so that, as time passes, the points A, B, C, D, lose their excitability in the order named. This statement holds good for excised *motor* nerves and for divided motor nerves in the body, and for undivided motor nerves at death. The further statement has been made that *sensory* or afferent nerves progressively lose their excitability in a reverse direction, *i.e.* from peripheral part first in a centripetal direction to central part last. The statement is purely conjectural, and not justified by experimental facts; it is not possible to test the point after death, and clinical experience teaches that the central end of a divided nerve can preserve its excitability for years.

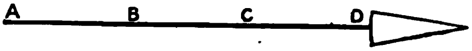


FIG. 164.

Fatigue of nerve?—'Fatigue'—the consequence of previous exertion of force—is caused by an actual expenditure of material, and accumulation of waste product, and has as its functional characteristic a diminished capability for renewed exertion. That muscle is a force-producing organ is recognised by the mechanical, thermic, chemical, and electrical changes that accompany contraction, and we have already recognised the signs of fatigue on excised muscle subjected to direct excitation (p. 332). We have now to examine nerve. In this case there is no mechanical change, nor have any thermal or chemical changes been detected consequent upon activity, the only recognised sign of activity in nerve itself being the negative variation. Whereas with muscular activity the evolution of heat, of carbon dioxide, of an acid, &c., are clearly demonstrable, with nervous activity nothing of the kind can be detected. Nerve is chiefly a force-conducting organ, and in very slight degree, compared with muscle, a force-evolving organ. Consequently, as may be expected, fatigue in nerve, as compared with fatigue in muscle, must be very slight; muscle can without difficulty be experimentally fatigued and exhausted; nerve is practically inexhaustible, and no proof has yet been given that nerve can suffer fatigue.

Diminishing muscular contraction consequent upon prolonged stimulation of the nerve of a nerve-muscle preparation, is no proof of fatigue of nerve. If the nerve-impulse be blocked by a constant current led into the nerve between the point of stimulation and the muscle, while the nerve of a second nerve-muscle preparation is also being stimulated, it will be found that the first nerve retains its excitability long after the second nerve has ceased to act upon the muscle—a proof that the exhaustion in this case is not of the nerve, seeing that the first nerve, though excited as long as or longer than the second nerve, retains its excitability, and can manifest it on its muscle whenever the block of the constant current is suspended (Bernstein). A curarised cat, after a sciatic nerve has been kept under excitation for hours, exhibits muscular contractions from the excited nerve as the curare effect wears off. (Bowditch.)

It must not, however, be concluded that the muscle itself is exhausted when stimulation of its nerve no longer causes it to contract. A direct stimulus to the muscle shows at once that it is still excitable. We have just seen by experiment that the nerve is still excitable. Seeing that stimulation of an excitable nerve fails to cause contraction of an excitable muscle, the conclusion follows that it is at the junction between nerve and muscle (the motor end-plate) that fatigue and exhaustion first develop. The actual nature of the feeling of fatigue, and the relative shares in it assumed by peripheral and by central changes, will be more suitably discussed in connection with cerebral function (p. 550).

CHAPTER XI

* *ANIMAL ELECTRICITY*

PAGE
379 Galvani—Volta—Du Bois-Reymond—Hermann.
381 The electromotive properties of muscle and nerve—Normal muscle is isoëlectric —Local injury disturbs this state—Local action disturbs this state—The negative variation of muscle—of nerve—The double or diphasic variation.
386 Experiments on man—Du Bois-Reymond's experiment—Hermann's experiment.
387 The frog's heart—The mammalian heart—The human heart.
389 The contraction without metals—The secondary contraction.
390 Cutaneous currents — Glandular currents — The submaxillary currents— Cerebro-spinal currents— Retinal currents.
393 Electrical fishes.

Animal electricity may be regarded as having taken origin from the observation by Galvani of the spasms occurring in frogs' legs which were suspended by copper hooks to an iron balustrade (1790). We now know that such spasms are not evidence of animal electricity, but caused by currents arising from dissimilar metals. A long controversy between Galvani and Volta, supported by numberless experiments from the roughest to the most precise, a new and delicate instrument—the galvanometer —the outcome of discoveries in the collateral subject of magnetism, were however required before any clear understanding was reached. From the outset Galvani asserted the existence of animal currents, and denied that of metal currents; Volta denied the existence of animal currents, and asserted that of metal currents. We now know that both assertions are correct, both denials incorrect. Animal currents exist, metal currents exist; the latter in Volta's hands were the seed out of which have sprung the battery, the telegraph, the electric motor, the electric light, and the telephone; the former in Galvani's hands is the parent of the more hidden offspring, animal electricity, or the electricity evolved by living tissues.

It will be useful to repeat, as may easily be done, the chief landmark experiments to which appeal has been made during the growth of animal electricity, and by which certain simple conclusions have been isolated.

1. *Galvani's first experiment* (*with metals*).—Pith a frog and remove the skin, lay bare the long roots of the sciatic nerves, take away the intestines and other soft parts, leaving only a piece of vertebral column and the nerves, by which the legs can be suspended with a copper hook to an iron stand; tilt the stand until one of the legs touches the iron. Contraction occurs. This contraction is due to a completion of circuit allowing of the sudden passage of a current. Galvani thought the current was from the animal, Volta objected that it was from the contacts with copper and iron. In the controversy which followed Galvani showed that two metals were not necessary to the success of the experiment; Volta objected that even a single metal differs at different points, and may, therefore, give a current.

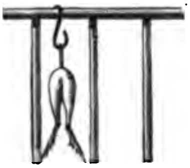


FIG. 165.—GALVANI'S EXPERIMENT WITH METALS.

2. *Galvani's second experiment* (*without metals*) gives however proof positive that animal tissues and fluids can produce and conduct a current, and is to be regarded as the foundation-stone of animal electricity. A nerve-muscle preparation is laid upon a glass plate, the nerve is raised upon a glass rod, and its extremity is allowed to touch the muscle, when a contraction occurs. Here the circuit is entirely animal tissue and fluid, and the current made through it at its completion must therefore be 'animal.'

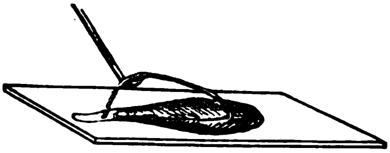


FIG. 166.—GALVANI'S EXPERIMENT WITHOUT METALS.

This really proved Galvani's assertion that animal currents exist, but it did not prove the non-existence of metal currents. Meanwhile Volta conclusively proved his assertion that metals in contact with a fluid produce a current; he invented the battery, and by his discoveries entirely overshadowed Galvani's successful demonstration.

In 1819 Oersted discovered and demonstrated the manner in which a magnetised needle is deflected by an electric current in its vicinity, and among the important consequences of the discovery was the invention and construction by Nobiling in 1825 of the galvanometer, which enabled subsequent observers to detect and measure the comparatively small currents derived from animal tissues.

In 1841, du Bois-Reymond began to devote himself to their study; by the invention of unpolarisable electrodes, and by his application of the method of compensation with the aid of the rheochord, he finally separated animal from metal currents, measured the former under various conditions of activity, and demonstrated the important phenomenon of the 'negative variation,' or, as it is now more usually called, the 'current of action.'

This brings us to the modern phase of the subject in which Hermann is the chief factor; he was and is the leading opponent of du Bois-Reymond's theory that natural currents pre-exist in normal resting tissues, and is the leader of the growing school by whom animal currents are considered to be the result of chemico-physiological inequalities caused by injury or by activity.

The electromotive properties of muscle and nerve.—Muscle and nerve may be conveniently considered together as regards their electromotive properties, for the principles upon which the phenomena are to be explained are the same for both, and the differences—which are of a minor character—can be easily understood after the facts common to both have been mastered. These facts may be briefly formulated in three propositions.

1. *Normal muscle (or nerve) is isoëlectric, i.e.* gives no current through a galvanometer with which it is connected by a pair of unpolarisable electrodes applied to any two points of the muscle (or nerve).

2. *Local injury disturbs this state;* current is manifested through the galvanometer from the uninjured to the injured part.

3. *Local action disturbs this state;* current is manifested through the galvanometer from the resting to the active part.

Of these three statements the first has been the most disputed and cannot well be completely demonstrated, the last two are easily verified.

Perfectly 'normal' muscle, *i.e.* muscle at rest and free from injury, cannot be experimented upon because the necessary exposure is a sufficient cause of injury, and exposure is necessary because the skin, if it be not removed, itself gives current. This is true of all animals, including fishes. But that 'normal' muscle, if it could be examined, would be found to be isoëlectric or currentless, is practically certain; the heart, which can be exposed without injury, is so, and muscle gives least current when it is exposed with most care, *i.e.* with least injury. Further the effect of local severe injury intentionally caused, gives a comparatively strong current, and it is highly probable that the comparatively weak currents observed from a carefully exposed muscle, are due to local slight injuries incidental to exposure. The direction of current when a local injury is inflicted is best understood by comparing it with the case of the Daniell cell.

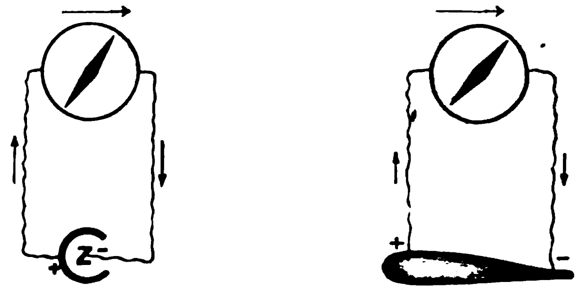


FIG. 167.

DIRECTION OF CURRENT OF DANIELL CELL.

Through the galvanometer the current is from copper to zinc.

Through the cell the current is from zinc to copper.

DIRECTION OF CURRENT OF INJURED MUSCLE.

Through the galvanometer the current is from normal to injured part, or from resting to active part.

Through the muscle the current is from injured to normal part or from active to resting part.

The injured muscle is thus an electromotive element, comparable with a Daniell cell, and just as in the latter the zinc, at which most chemical action takes place, is the positive element, and has connected with it the negative electrode, so in the former the injured part, at which most chemical action takes place, is a positive element, and has connected with it a negative electrode. It is usual to describe direction of current with reference to its passage through the galvanometer, and to say that B, the injured part, is negative to A, the normal part. The expression 'negativity of injury' is sometimes used to express this relation of B to A.

A precisely similar mode of explanation is applicable to the effect of *local action.* At the seat of action most chemical change takes place; the active part is thus analogous with the zinc of the Daniell element, and the current in the galvanometer is from part at rest to part in action, in the muscle itself from part in action to part at rest. Describing direction of current with reference to its passage through the galvanometer, we say that

B, the active part, is negative to A, the resting part. The expression 'negativity of action' is sometimes used to express this relation of B to A. These considerations apply equally to muscle and to nerve.

The negative variation of muscle (*or of nerve*).—If an injured muscle giving the injury current from A to B, be tetanised

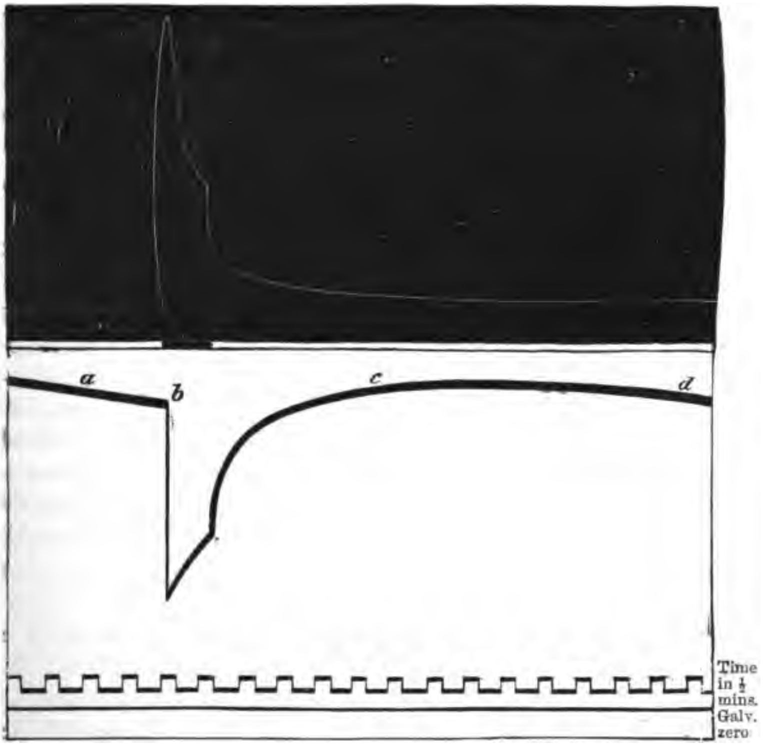


FIG. 168.—THE NEGATIVE VARIATION. (Frog's Gastrocnemius.)

Simultaneous record of a tetanic contraction (white line) and of the accompanying negative variation of a current of injury (black line). (*a*) The current of injury is normally subsiding; (*b*) it is suddenly diminished during tetanus (negative variation); (*c*) it subsequently increases (positive after-variation); and (*d*) it finally resumes its normal decline.

by excitation of its nerve, tetanus will include its whole mass, but the change from rest to action will be greater at the uninjured part A than at the injured part B, *i.e.* there will be an action current from B to A which, while the muscle is tetanised, will diminish the injury current from A to B. This diminution is the '*negative variation.*' A single muscular contraction is sufficient to give a negative variation, but tetanic contraction will bring it into stronger evidence.

Seeing that a simple negative variation as above described depends upon greater action at an uninjured point A than at an injured point B, it is easy to see that the negative variation will be greater with greater current of injury. The negative variation in muscle appears to precede the contraction to which it belongs, as may be best observed in the heart. (See fig. 171.) We have said 'appears to precede' because there can be no doubt that under ordinary conditions the mechanical event really begins before it becomes visible, and it is possible that it actually begins with and not after the electrical event. In the case of voluntary muscle no interval is demonstrable; both events have a latent period as short as $\frac{1}{400}$ sec. (B. Sanderson.)

Characters of the negative variation.—The negative variation in nerve quickly reaches a maximum with increasing strength of stimulating current, is not reversed in direction with reversal in the direction of the stimulating current, does not vary in magnitude with increasing interval between the stimulated and led-off regions of the nerve, and is abolished by ligature in that interval. By the first three of these signs it is distinguished from electrotonic currents; the last is common to both. According to Sanderson and Gotch the negative variation of potential accompanying a muscular contraction may exceed the potential difference due to injury, *e.g.*, 0·08 volt in the former case as compared with 0·04 in the latter.

The double or diphasic variation.—Whereas the presence of a strong current of injury is favourable to the demonstration of the simple negative variation, which is the sign of the unbalanced negativity of action in the uninjured tissue, it is unfavourable to the demonstration of the diphasic variation which is a manifestation of the negativity of action, first at one part, then at another part of uninjured tissue. The most favourable organ for the demonstration of the diphasic variation is the frog's heart, it is less easy to demonstrate upon an ordinary muscle, it is most difficult upon nerve. The double variation depends upon the fact that action is not simultaneous throughout the whole mass of a muscle, but occupies time in its transmission from a point of stimulation.

If A and B be electrodes applied to an *uninjured* muscle, C the point of application of a stimulus, the part at and near A will commence to act and become negative *before* the part at and near B; during the interval between the commencement of action at A, and that subsequently at B, the negativity of A is unbalanced; this constitutes the first phase. The part at and near B will continue active and remain negative *after* the part at and near A has ceased to be active, during the interval between the cessation of action at A and that subsequently at B the negativity of B is unbalanced; this constitutes the second phase. Between the first and second phases, while A and B are both active and negative, the negativity of A more or less accurately balances that at B; this constitutes the isoëlectric interval. Now it is obvious that the slower the transmission of the active negative state from A to B, the more opportunity there is for the manifestation of unbalanced negativity, at A when the process begins, and at B when it ends. Hence it is most easy to demonstrate on the frog's heart in which the active state travels at the rate of $\frac{1}{10}$ meter per second, less easy on muscle in which the rate of transmission is not less than 1 meter, most difficult on nerve in which the rate of transmission is about 30 meters. The diphasic variation in cooled nerve is however easily observed, the rate of transmission being then reduced to about 1 meter per second.

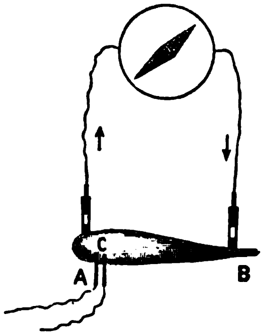


FIG. 169.

We may illustrate the mechanism of a diphasic variation by the following analogy. A railway train (=a nervous impulse) 50 meters long running at a speed of 50 meters per second, works two signals A and B at 10 meters from each other, which fall while the train is at points opposite them, but rise again when the train has passed. During a first period the train is at A and not yet at B, and A is negative to B (1st or initial phase). During the second period the train is opposite A and B, which are both negative (isoëlectric interval). During a third period the train is past A but still at B, and B is negative to A (second or terminal phase). With the speed and distances given above

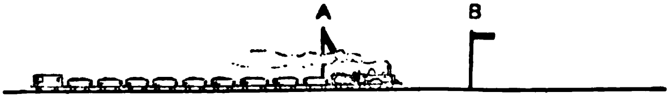


FIG. 170.

the initial phase would last $\frac{1}{5}$ sec., the interval $\frac{3}{5}$ sec., and the terminal phase $\frac{1}{5}$ sec. Bearing in mind that in a nervous impulse there is no actual transport of matter, but only the propagation of a motion, this figment usefully represents the diphasic and some other of the electrical changes taking place in nerve or muscle—*e.g.* if there is an injury at B, B will be negative to A (current of injury); if a continuous or tetanic series of impulses passes when B is down, A only will fall (excitatory diminution of current of injury); if a continuous series passes when there is no injury, both A and B will be kept down: if impulses pass in an opposite direction, the direction of the phases will be reversed, &c.

Experiments on man.—Two different experiments relating to the electromotive action accompanying muscular contraction, have been made upon the human subject—one by du Bois-Reymond relates to voluntary tetanic contraction, the other by Hermann to tetanic contraction caused by electrical stimulation.

Du Bois-Reymond's experiment.—Each of both hands are led off to a galvanometer by two vessels into each of which a finger is dipped. The voluntary contraction of the muscles of either arm gives a deflection which indicates the passage of a current through the galvanometer from the passive to the contracting arm, and through the body from the contracting to the passive arm—*i.e.* negativity of the active side. Objection has however been taken to the view that the negativity is due to muscular action, and it has been attributed to cutaneous secretory action; it has been found that on a curarised cat, excitation of the sciatic, while causing no muscular contraction, gives the current above described, while on an atropinised cat excitation of the sciatic causes muscular contraction but no action current.

Hermann's experiment.—The forearm is led off to a galvanometer by two bracelet electrodes; muscular action is provoked by electrical excitation of the brachial plexus, and the rheotome is employed. A series of observations is taken, the rheotome being shifted from zero (simultaneous excitation and rheotome closure) onwards, and demonstrates the presence of a diphasic variation. The phases are such as to indicate: 1, negativity of muscle proximal to the nerve entrance; 2, negativity of muscle distal from such nerve entrance. The phenomenon is far more rapid than on frogs' muscle, and time-measurements give for the rate of propagation of the excitatory state (negativity) a value of about 12 meters per second.

Experiments on the heart.—*The frog's heart.*—On the frog's heart the normal diphasic variation of its spontaneous systole is as follows:—first phase, base negative to apex; second phase, apex negative to base. If the heart be stanniused and stimulated at the base, the two phases of the consequent contraction are the same as with the spontaneous beat; but if the stimulus be at the apex, the two phases are reversed, *i.e.* in the first phase, apex is negative to base; in the second phase, base is negative to apex. Obviously this is owing to contraction commencing at apex and extending to base.

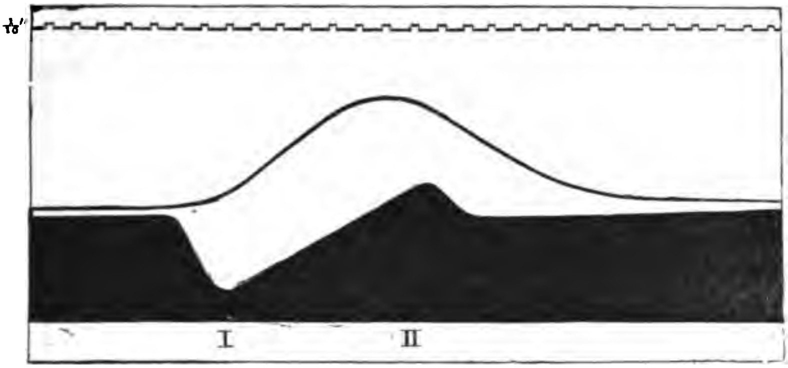


FIG. 171.—FROG'S HEART. DIPHASIC VARIATION.

Simultaneous photogram of a single beat (black line) and of the accompanying electrical change indicated by the level of the black area, which shows the varying level of mercury in a capillary electrometer. The base of the ventricle is connected with the mercury. I. First phase, base negative to apex. II. Second phase, apex negative to base.

The electrical variations of the excised mammalian heart are essentially similar; the normal accompaniment of the spontaneous beat is a diphasic variation in which the two phases are usually such as to indicate: 1, negativity of apex; 2, negativity of base. But exceptions to this rule are not uncommon. If, for instance, the apex is injured, the apex phase fails, and the base phase appears alone and increased; if the base is injured, the base phase fails, and the apex phase appears alone; the sequence can be reversed at will by alterations of temperature, and, according to Bayliss and Starling, the sequence of the heart *in situ* is 1, base; 2, apex.

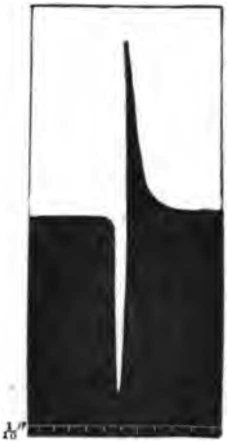


FIG. 172.—CAT'S HEART. DIPHASIC VARIATION.

By stimulating a normal quiescent ventricle a double variation is produced, just as in the frog's heart, being $\left\{\begin{array}{l}\text{1. A negative}\\ \text{2. B negative}\end{array}\right\}$ if the stimulus is at A, or $\left\{\begin{array}{l}\text{1. B negative}\\ \text{2. A negative}\end{array}\right\}$ if the stimulus is applied at B.

The human heart.—The electrical variations of the mammalian heart may also be studied upon intact animals and upon man by means of Lippmann's capillary electrometer (p. 314). By means of this instrument variations of electrical potential which are associated with the beat of the human heart can be demonstrated, and their mode of distribution in the body determined, by simply 'leading off' from various points of the surface. This mode of

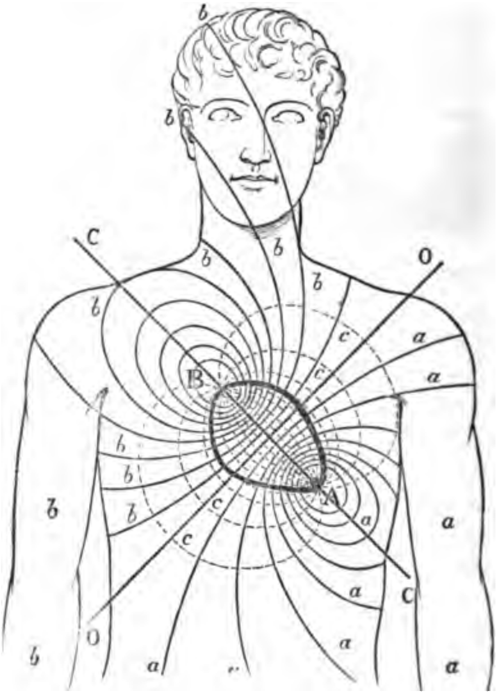


FIG. 173.

Let A and B respectively represent apex and base of the ventricular mass. Then, if at any moment a difference of potential should arise between A and B, a current *c c c* will be established along and around the axis A B. The line O O will represent the plane of zero potential or equator. The lines *a a a*, *b b b* will represent equipotential curves around A and B. A difference of potential between A and B will be manifested if the two leading off electrodes are applied on opposite sides of the equator O O; no such difference will be manifested if both electrodes are on the same side of the equator. Transferring these data to the human body, it is clear that the equator O O will divide the body into two asymmetrical parts, (1) a portion *b b b* including the head and right upper extremity, (2) a portion *a a a* including the three other extremities.

distribution will best be understood by reference to the accompanying diagram and description.

If we lead off to the electrometer by any two points *a* and *b* on opposite sides of the equator, we shall see the mercury pulsate with each beat of the heart; if we lead off to the electrometer by any two points *aa* or *bb* on the same side of the equator, the electrometer will not be affected by the heart-beat.

The electrical effects, obtained in the first series of observations, *i.e.* with the electrodes applied on opposite sides of the equator, if examined by the aid of photographic records, show :—

1. An initial phase preceding the systole, during which any point of the surface *a* is negative to any point of the surface *b*. 2. A terminal phase preceding the diastole, during which any point *b* is negative to any point *a*.

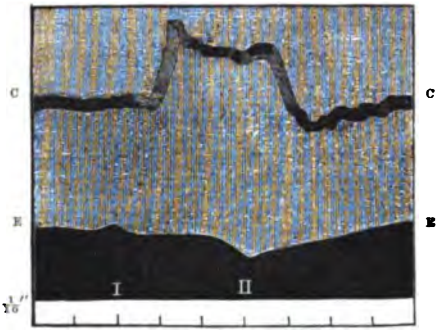


FIG. 174.—HUMAN HEART. DIPHASIC VARIATION, E E; AND SIMULTANEOUS CARDIOGRAM, C C.

The leads off to the capillary electrometer were from the mouth to the mercury, and from the left foot to the sulphuric acid.

According to the recent observations of Bayliss and Starling, the initial phase is itself double, so that the order of negativity is in reality $b-a-b$, and not $a-b$. A similar triphasic variation, $b-a-b$, in place of the ordinary variation, $b-a$, is often to be observed in the spontaneous beat of the frog's heart, the final *b* phase being presumably due to the contraction of the bulbus arteriosus. It is therefore probable that in all kinds of hearts the contraction begins from the base, spreads to the apex, and ends at the base.

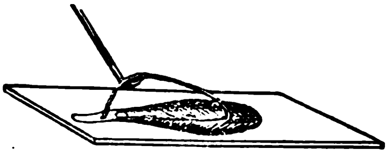


FIG. 175.—GALVANI'S EXPERIMENT WITHOUT METALS.

The contraction without metals.—If the nerve of a nerve-muscle preparation be suddenly dropped upon another muscle (or upon the muscle of the preparation itself), preferably so as to touch an uninjured and an injured part, it will be excited and its muscle will contract. The excitation is due to the injury-current of the muscle upon which the nerve is dropped, suddenly made through the nerve; the experiment is most likely to succeed if the nerve is dropped across a longitudinal surface and a freshly-made transverse section.

The *secondary contraction* is caused by a current of action; if while the nerve of II is resting upon the muscle I, the latter be caused to contract by excitation of its nerve, the sudden electrical variation accompanying the contraction of I will stimulate the nerve of II and cause a contraction of the muscle II. This is the secondary contraction.

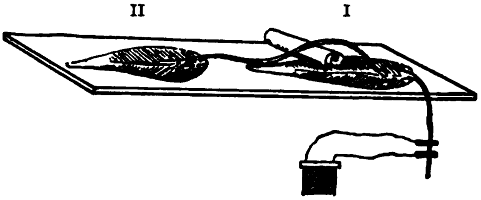


FIG. 176.—THE SECONDARY CONTRACTION.

Secondary contraction from the heart is obtained when the heart is substituted for the muscle I. Just before the commencement of each beat, the nerve of II is excited by the electrical variation which belongs to the contraction of the heart and the muscle II contracts. Under favourable circumstances (*i.e.* with a very excitable nerve and an uninjured heart giving a diphasic variation) the muscle contracts at the end as well as at the beginning of the heart's contraction. Occasionally on decapitated animals, immediately after decapitation, the left side of the diaphragm may be observed to contract at each beat of the heart. This is due to excitation of the left phrenic nerve by the electrical variation with cardiac contraction, and is an instance of 'secondary contraction from the heart.' Kühne has shown that if two muscles are pressed together, excitation of either will cause contraction of both; this is secondary contraction from muscle to muscle.

Cutaneous currents, glandular currents.—The skin of all animals, not excepting fishes, is in the normal state traversed by an electrical current from without inwards. In the skin of the frog, as well as in that of mammals and of man, this current is mainly caused by cutaneous glands. But that a cutaneous current is in part due to skin itself apart from its glands, is proved by the currents of fishes' skin (*e.g.* of the eel), which contains no glands. The purely cutaneous current, the electromotive force of which is ·003 to ·007, is according to Hermann attributable to the degenerative action or partial death which accompanies the formation of the epidermis.

The cutaneous gland-current or so-called secretion-current is likewise directed from without inwards. It is increased by excitation of secreto-motor nerves, *i.e.* it gives a positive variation. The best-known instance of a cutaneous gland-current under the influence of secreto-motor nerves, is that which is afforded by the pad of the cat's foot, where excitation of the sciatic nerve causes an outbreak of sweat accompanied by a positive variation of the skin-current, effects which are no longer produced after the administration of atropin. The current obtained in du Bois-Reymond's experiment on man is according to Hermann of a similar nature, *i.e.* a gland-current directed from without inwards in the skin of the active hand. According to Tarchanoff, the cutaneous currents of man are exceedingly sensitive, especially in parts of the skin where the sweat-glands abound, being increased by all kinds of cerebral activity in the absence of visible muscular contractions.

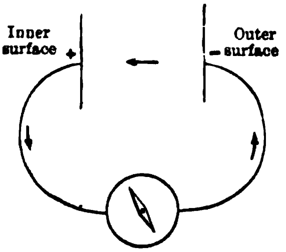


FIG. 177.—SKIN CURRENT.

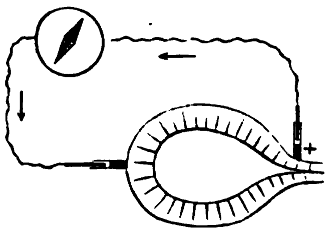


FIG. 178.—GLAND CURRENT.

The submaxillary gland is also the seat of a glandular current which according to Bayliss and Bradford is directed from without inwards, or in the galvanometer circuit from hilum to surface, and which is increased by excitation of the chorda tympani (positive variation), diminished by excitation of the sympathetic (negative variation).

Cerebro-spinal currents.—According to Setschenow, the medulla oblongata of the frog, if led off to the galvanometer, exhibits irregular series of electrical variations which may be excited or arrested by excitation of the central end of the sciatic. Caton has published observations to show that visual excitation causes electrical effects in the cortex cerebri. Gotch and Horsley have recently led off the electrical signs of nerve action from the white columns of the spinal cord, by means of the capillary electrometer. The instrument applied to motor paths yielded an exact reproduction of the muscular response, *i.e.* it indicated the character of the downward impulses, and may therefore be appealed to as a trustworthy indicator of the passage of the upward impulses which can otherwise only be studied by their reflex effects. More recently still Beck has made observations similar to those of Caton; and v. Fleischl, in consequence of the results said to have been obtained by Beck, has published observations relating to the cerebral currents on man. There is no doubt that the current of action can be demonstrated in the *white* matter of the cord as in a nerve-trunk; its manifestation by the grey matter of nerve-centres is still *sub judice*.

Retinal currents.—If two unpolarisable electrodes connected with a galvanometer are connected with an excised frog's eye, one with the cornea, the other with the optic nerve, a deflection is obtained showing that the optic nerve is negative to the cornea. This is an ordinary current of injury arising from the cut optic nerve, and not assignable to the retina. If now all light is cut off from the eye by a shutter, the current is sometimes diminished, but more often increased (negative or positive variation). If on the contrary the shutter is opened and the eye subjected to ordinary daylight, or better to a strong beam of artificial light, the current is usually (but not always) increased. In other words the impact of light usually causes a positive variation; the removal of light causes a positive or a negative variation of the current of injury.

An entirely satisfactory explanation of these effects cannot be given, but the important fact remains that light acting upon the retina causes an electrical change which is the physical token of retinal activity. Holmgren showed by exclusion that the electrical variation caused by light depends upon the retina only, and is not due to the action of light upon any other constituent of the eyeball; nor is it due to changes of pigment; he showed also that the external or choroidal surface of the retina is negative to its internal surface. Kühne and Steiner found that the variation occurs nearly as well on a retina devoid of visual purple, as on a non-bleached retina, although its character was somewhat different in the

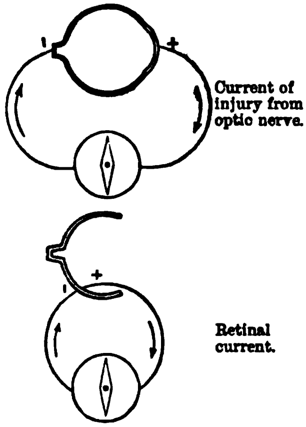


FIG. 179.—EYE CURRENTS.

two cases. Dewar and McKendrick found that white or coloured light acted upon the retina in the following order of strength—white, yellow, green, red, blue. They also demonstrated the electrical variation on intact animals and on man, one electrode being on the eye, the other on any other part of the body. With regard to the magnitude of the change, they estimated it at $\frac{1}{10000}$ Daniell. The essential phenomenon is the current of action; whether or no a current pre-exists due to injury or other accidental conditions, is a matter of secondary importance.

The most striking manifestations of animal electricity are those which are afforded by electric fishes—*gymnotus*, *torpedo*, and *malapterurus*. Their electric organs are practically powerful batteries, from which a succession of instantaneous discharges of high intensity can be liberated at will of the animal, or in a reflex manner by cutaneous stimulation, or experimentally by direct electrical excitation of the organ itself or of its efferent nerves. In the torpedo the electrical organ is in the shape of two lateral masses composed of numerous hexagonal prisms perpendicular to the surface of the body, these prisms being subdivided into compartments by transverse septa parallel with the surface. In the discharge of the organ the current flows from the dorsal to the ventral surface through the galvanometer,

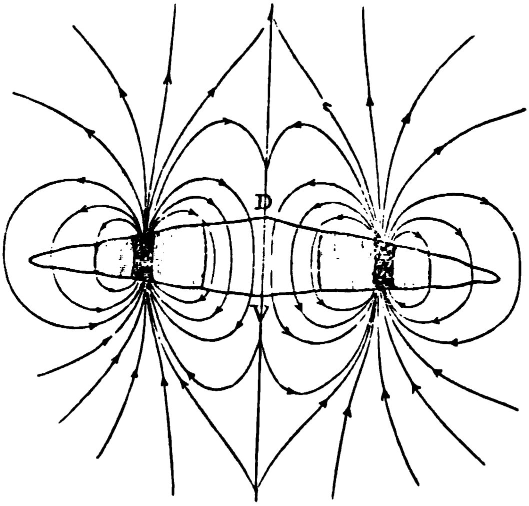


FIG. 180.—DIAGRAMMATIC TRANSVERSE SECTION OF TORPEDO.
D dorsal, V ventral surface; Direction of discharge indicated by arrows.
(Du Bois Reymond.)

from the ventral to the dorsal surface through the organ itself. According to du Bois-Reymond the electrical resistance of the living organ is very much greater to *down* currents from dorsal to ventral surface than to *up* currents from ventral to dorsal surface. According to Gotch this apparent difference is the effect of an upward action current adding to the up current and subtracting from the down current.

In the gymnotus the shocks are always directed from tail to head in the animal, in the malapterurus they are directed from head to tail. The direction, as was pointed out by Pacini, depends upon the points of entrance of the electric nerves; in torpedo they are distributed to the ventral surface, in gymnotus to the posterior surface, and in malapterurus to the anterior surface of the organ. The discharge is always such that the nerve surfaces are active, *i.e.* analogous with the zinc of a Daniell cell. The discharge is a discontinuous one, composed of as many as 200 shocks per second in the fresh condition, but, with exhaustion, falling in frequency and in force. A single shock has a latent period of about $\frac{1}{200}$ second, and a duration of $\frac{7}{100}$ second. The rate of transmission along the electrical nerves is about 7 meters per second; the fish themselves are unaffected by electrical currents sufficient to kill non-electrical fish.

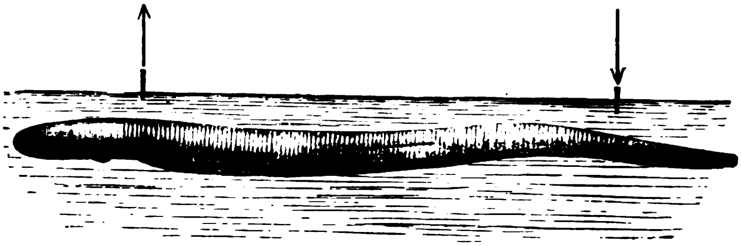


Fig. 181.—Gymnotus.

Direction of discharge indicated by arrows and leading off electrodes from water.

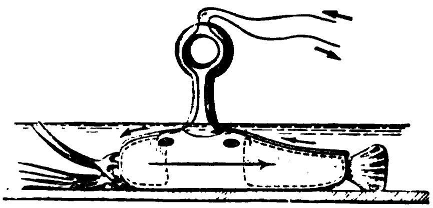


Fig. 182.—Malapterurus.

Led off by two shields, discharge indicated by arrows. (Du Bois-Reymond.)

CHAPTER XII

LIGHT AND VISION

PHYSICAL DATA

LIGHT

PAGE
396 **Reflection—Refraction**—Index of refraction—The prism.
397 *Lenses*—Foci—Principal focus—Conjugate focus—Real focus—Virtual focus Centre of curvature—Optical centre—Principal axis—Secondary axis.
399 Images—Real reversed and virtual erect—Mirror images.
399 Spherical aberration—Chromatic aberration.
400 Lens units—The Diopter.

COLOUR

401 Composition and decomposition of white light.
401 Complementary colours—Differences of colour—Tone, saturation, and brightness—* The colour triangle—Young-Helmholtz theory—Hering's theory.
407 Colour-blindness—The colour-perimeter.

THE EYE

408 Iris—Pupil—Retina—Refractive media—The lens.
411 **Listing's reduced eye**: Nodal point—Optic axis—Line of vision—Visual angle—Optical problems.
414 **Accommodation**: Ciliary muscle—Far point—Near point—Range of accommodation—Variations with age—Myopia, hypermetropia, and presbyopia —Sanson's images.
420 The field of vision—The perimeter.
420 Scheiner's experiment.
422 Astigmatism—Irradiation.
424 Relation of retina to field of vision—Hemiopia and hemianopsia.
425 'Corresponding points'—The Horopter.*
428 Double vision or 'Diplopia'—Double vision from squint.
429 Movements of the eyeball—Movements of the iris.
436 Retinal shadows—Of foreign bodies—of blood-vessels.
439 Phosphenes.
440 **Objective effects of light upon the retina**—Bleaching—Movements of pigment —Movements of cones—Electro-motive changes.
442 **The Ophthalmoscope**: Indirect method—Direct method.
445 Relation of light perception to retinal stimulation—After images—Positive and negative; retinal fatigue.
448 **Contrast**: Simultaneous and successive—Colour contrasts.
451 Binocular effects.

Reflection.—A ray of light falling upon a polished surface is *reflected* (fig. 183). The angle of incidence A B N is equal to the angle of reflection N B C, B N being the normal or perpendicular to the reflecting surface S S at the point of incidence B.

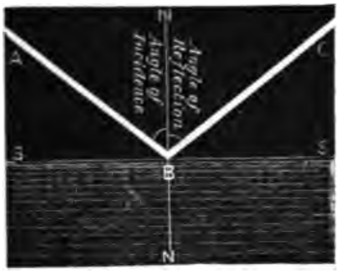


FIG. 183.—REFLECTION.

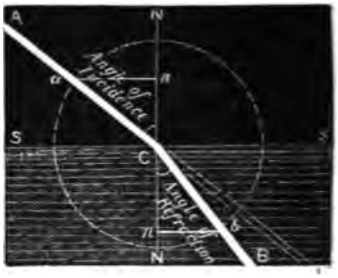


FIG. 184.—REFRACTION.

S S, boundary surface between air and glass. N N, perpendicular to the surface, S S. A ray of light passing in the direction A C B is deflected towards N N in passing from air to glass. A ray of light passing in the direction B C A is deflected from N N in passing from glass to air. A C is the incident ray. C B is the refracted ray.

Refraction.—A ray of light passing from a medium of less density into one of greater density, or *vice versâ*, is bent or *refracted* from its original direction (except its direction be perpendicular to the surface of contact between the two media). Passing from a medium of less to one of greater density, *e.g.* from air to glass, the ray is refracted towards the normal; passing from a medium of greater to one of less density the ray is refracted away from the normal.

Index of refraction.—The relation $\frac{\text{sin. angle of incidence}}{\text{sin. angle of refraction}}$ or $\frac{a\,n}{b\,n}$ is the *index of refraction* of the substance into which the ray passes from air. It is constant for all angles of incidence, but various for various refracting media. Of glass the index of refraction is 1·5 to 1·6, according to the kind of glass.

Of water	1·33
„ crystalline lens	1·40 to 1·45
„ vitreous body	1·34
„ aqueous humour	1·34

If the ray pass through a glass plate with parallel surfaces (fig. 185), it is bent towards the perpendicular at B, from the perpendicular at C. Its direction from C to D is parallel with its direction from A to B.

If the ray pass through a glass prism (fig. 186), it is refracted at B towards the perpendicular N, and at C from the perpendicular N—*i.e.* in each case towards the base of the prism.

A pair of prisms joined by their bases will deflect rays, in the same plane, passing through each of the two prisms towards each other. A pair of prisms joined by their apices will deflect rays passing through each of the two prisms away from each other.

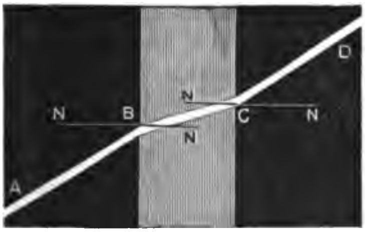


FIG. 185.—RAY THROUGH PLATE.

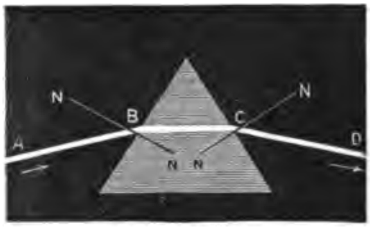


FIG. 186.—RAY THROUGH PRISM.

Lenses.—A biconvex lens may be regarded as composed of an infinite number of prisms with their bases towards the centre of the lens; its effect will be to cause rays of light to converge. A biconcave lens may be regarded as composed of an infinite number of prisms with their apices towards the centre of the lens; its effect will be to cause rays of light to diverge. The *focus* of a lens is the point of meeting of refracted rays (real focus), or of their prolongations backwards (virtual focus). The *principal focus* is the focus of rays parallel with the principal axis of the lens, and its distance from the lens is the principal focal distance.

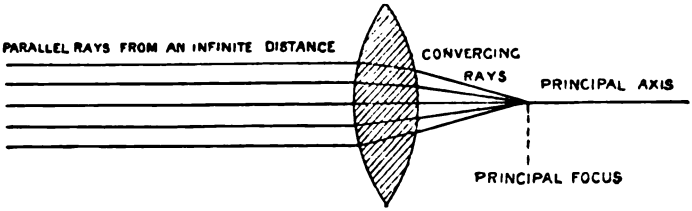


FIG. 187.

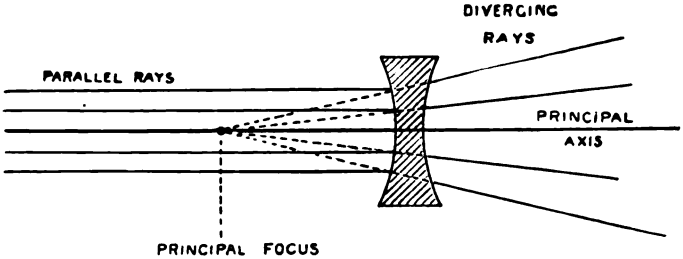


FIG. 188.

Conjugate foci.—A conjugate focus is the focus of divergent rays from a luminous point. C and C_1 (in fig. 189) are conjugate points. The principal and conjugate foci are *real* foci. A *virtual* focus is formed by a luminous point situated between the lens and its principal focus. The rays after passing through the lens are still divergent, their prolongation backwards to their point of intersection gives the virtual focus of the point. A concave lens causes divergence of the rays of light by which it is traversed, and has only virtual foci (fig. 188).

Centre of curvature.—A spherical surface—*i.e.* a surface forming part of a sphere—has a centre of curvature P which is the centre of the sphere. A straight line joining the centres of curvature of the two spherical surfaces of a biconvex lens is its *principal axis* (fig. 190). The point of the principal axis through which any luminous ray, S, passes without angular deviation, the emergent being parallel to the incident ray, is called the *optical centre* of the lens; any straight line, S, passing through the optical centre, without passing through the centres, of curvature, is a *secondary axis*.

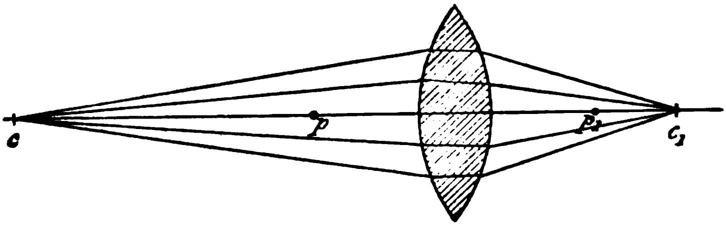


FIG. 189.

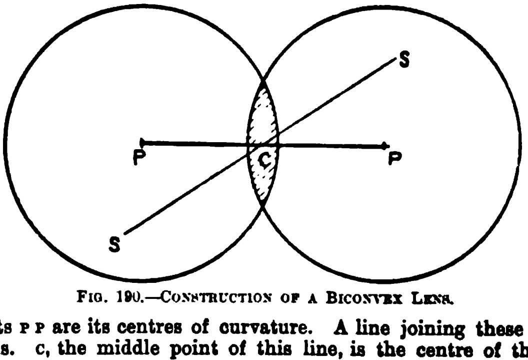


FIG. 190.—CONSTRUCTION OF A BICONVEX LENS.

The points P P are its centres of curvature. A line joining these points is the principal axis. C, the middle point of this line, is the centre of the lens; any line, S S, passing through C is a secondary axis.

Rays parallel with a secondary axis, or emitted from points situated on a secondary axis, form foci, just as do rays parallel with the principal axis, hence images can be formed.

The image of an object is the collection of the foci of its several points. A collection of real foci constitute a *real image*, a collection of virtual foci constitute a *virtual image.*

If an object be situated beyond the principal focus of a lens, it forms an image which is real and inverted. If it be far from the principal focus, the image is small and close to the principal focus. If it be near the principal focus, the image is large and distant from the lens. These two extreme cases are respectively illustrated by a camera or eye and a magic lantern. If the object be at the principal focus no image is formed. If it be between the lens and its principal focus, there is no real image formed, but a virtual image, erect and larger than the object. The nearer the object is to the principal focus, the larger and more distant its image. A real image may be projected on a screen (large), or received by the eye (small); a virtual image can only be seen when it falls on the eye.

Mirror images.—The rays reflected from convex mirrors are divergent, such mirrors can therefore have only virtual foci, and can only give a *virtual image,* which is *erect and smaller* than the object; the greater the convexity the smaller the image. Concave mirrors give a *virtual erect image* of an object which is situated between the mirror and its principal focus; a *real reversed image* of an object situated farther from the mirror than its principal focus; if the object is between the principal focus F and centre of curvature C, its image is larger than the object, and situated beyond the centre of curvature; and, *vice versâ,* if the object is situated beyond the centre of curvature, its image is smaller than the object, and situated between the principal focus and centre of curvature; the image and the object occupy 'conjugate' positions.

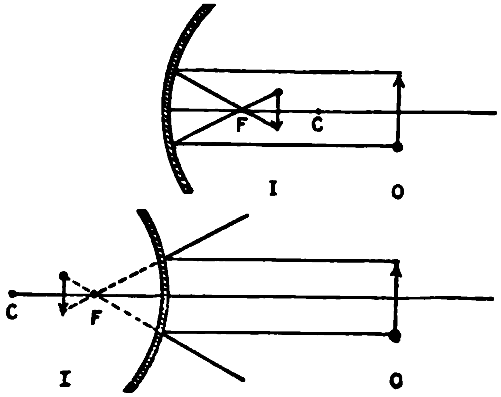


FIG. 191.

Sanson's images are mirror images from the cornea and lens. The first and second images are virtual and erect images reflected by convex surfaces; the third is a real reversed image reflected by a concave surface (p. 418).

Spherical aberration.—A spherical lens does not bring to an exact focus all the rays passing through it; rays passing through the central part of the lens are less strongly refracted than rays passing through parts further from the centre. This interferes with the distinctness of images, and is in part corrected by a diaphragm —*i.e.* a screen with a central aperture so that only central rays traverse the lens, and peripheral rays are arrested. In the crystalline lens of the eye, this is further corrected by a peculiarity of optical property—the refractive index is greatest at the centre.

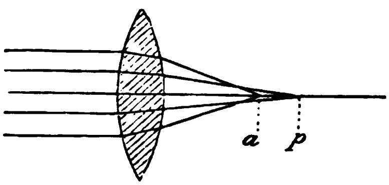


FIG. 192.—SPHERICAL ABBERATION.

Rays through central part of lens focussed at *a* in front of *p*, which is the focus of rays through border of lens.

Chromatic aberration.—A lens does not refract the constituents of white light in precisely equal degrees; it refracts rays of short wave-length more strongly than rays having greater wave-length—*e.g.* the violet more strongly than the red rays, so that the focus of violet rays is closer to the lens than that of red rays. Hence the image of a spot of light is apt to be surrounded by a red halo when the screen is rather within the mean focal distance of the lens, by a violet halo when the screen is rather beyond the mean focal distance of the lens. Chromatic aberration is an instance of the dispersion of white light by a prism into the colours of the spectrum.

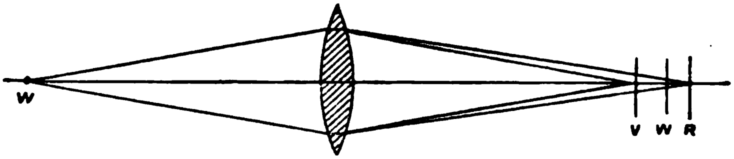


FIG. 193.—CHROMATIC ABBERATION.

Lens units. The diopter.—The stronger a lens, the shorter its focus, and *vice versâ.* The strength of a lens may therefore be indicated by stating its focal length—*e.g.* lenses of 1, 2, 3, &c. inches focal length are progressively weaker, their strengths being in the proportion 1, $\frac{1}{2}$, $\frac{1}{3}$, &c. This is, however, an inconvenient scale in actual practice, as, for instance, in the numeration of spectacle lenses, or in the estimation of the refraction of the eye.

It is more convenient to adopt as the unit a weak lens, viz. a lens with a focal distance of 1 meter. This unit is called the *diopter*, and is written 1 D. A lens twice as strong has a converging power equal to two such lenses, its strength is expressed as 2 D, and its focal distance will be $\frac{1}{2}$ meter. A lens ten times as strong has a converging power of 10 D, its focal distance is $\frac{1}{10}$ meter, *i.e.* 10 cm.

The focal value of concave lenses is similarly expressed with the negative sign prefixed, for the value of convex lenses the positive sign is commonly prefixed; thus $+n$ D is the power of a convex lens, $-n$ D is the power of a concave lens.

Colour[1]

White light is composed of many kinds of light—red, orange, yellow, green, blue, violet—and intermediate between these named colours innumerable others. This fact is demonstrated by interposing a prism on the path of a pencil of sunlight. Refraction occurs, being greatest for violet rays, least for red rays; the white light is decomposed into its constituent colours, and a continuous spectrum of the prismatic colours is obtained.

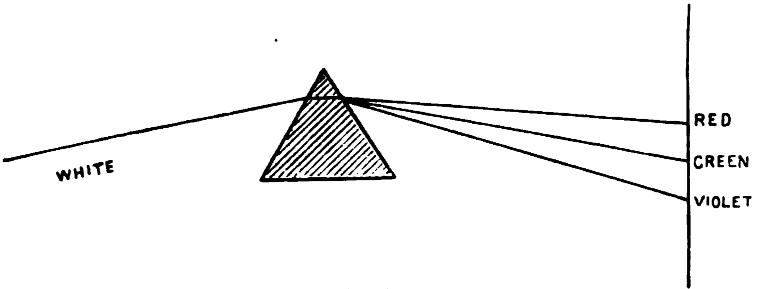


FIG. 194.

White light may be recomposed from its constituents, either *physically*, as by a second prism reversing the dispersion produced by the first prism, or *physiologically*, by causing the prismatic colours to fall upon the retina in sufficiently rapid succession. The readiest method of studying the effects of different colour mixtures is by means of a revolving disc to which two or more coloured discs are fixed, overlapping more or less, so that varying proportions of the colours occupy the entire circumference of the disc (Maxwell).

White light is composed of an infinite number of simple colours; it can, however, be produced by mixture of the three primary colours, or even of only two colours in certain proportions, but in this case one at least of the two colours must be other than a primary. Any two colours which taken together in proper proportions form white are called *complementary*. The complementary pairs of colours as above are roughly

---

[1] The simplest physical data concerning colour directly involve a physiological factor, inasmuch as the retina is the instrument of investigation. We shall therefore include theories of colour vision in this connection in order to avoid repetition. The subject is, however, more suitable for a second reading after the physiology of the retina has been studied.

Red and Green,
Orange and Blue,
Violet and Yellow,

a relationship which is indicated in the simple colour circle, complementary colours being at the opposite ends of the three diameters, R. G., O. B., Y. V.

Colours and their relation to each other and to white may, however, be more accurately represented on an incomplete curve forming the two sides of a triangle than on a complete circle as above. To understand the construction of the colour triangle, we may imagine the force or stimulation energy of colour to be represented by weights. If each colour were an equal force, then each of the colours R. O. Y. G. B. V. would be represented by equal weights at equal intervals on the circumference of the circle, and the resultant of their fusion would be at W., their centre of gravity—*i.e.* the centre of the circle. But this is not the case; the component colours of white light are not of equal stimulation energies, and may not therefore be represented by equal weights. These differences are taken into account in the construction of a colour triangle, which gives the colours as if represented by weights proportional to their stimulation energies, white as the resultant of their fusion being at the centre of gravity of the system. A properly constructed colour triangle exhibits, moreover—(1) the relative strengths of the different colours, these strengths varying inversely as the distances from W.; (2) the position of complementary colours, these being situated at opposite ends of straight lines drawn through W. to the boundary of the triangle; (3) the position of mixture colours, these being on the straight line joining the positions of the constituent colours—*e.g.* mixtures of the red and green being on the line R. G., of green and violet on the line G. V., of orange and blue on the line O. B.; (4) that the primary colours R., G. and V. being at the angles of the triangle, are not producible by mixtures of any of the other colours. The broken

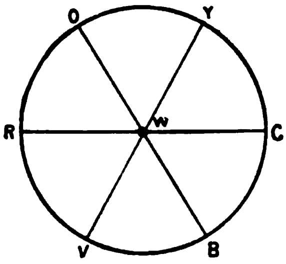


FIG. 195.—COLOUR CIRCLE.

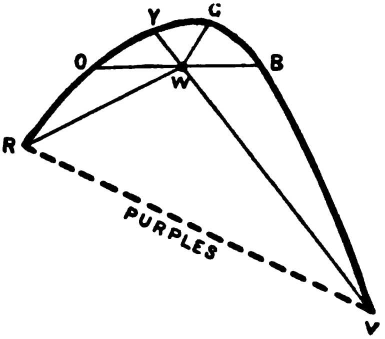


FIG. 196.—COLOUR TRIANGLE.

line forming the base of the triangle between R. and V. expresses the fact that the spectrum does not return upon itself, and cannot therefore be represented by a closed curve, but that a series of non-spectral purples exist in nature, grading from red to violet, complementary to green and to the neighbouring colours at the apex of the triangle.

Differences of colour are of three kinds :—

1. Tone or wave-length.
2. Saturation or fulness.
3. Brightness or strength.

It is easier to show by examples what is meant by these terms than formally to define them. We cannot, for instance, express the energy values of two different colours in terms of a common unit, and we are very liable to confuse physical measures of the stimulus with physiological measures of the sensation.

The pairs of terms given above are those generally used as synonymous; but we may advantageously distinguish between the terms 'brightness' and 'strength,' for instance, as regards their application to light and to colour. We ought to apply 'brightness' to the *sensation*, 'strength' to the *stimulus*, just as we apply 'sweetness' to the sensation of a sugar solution, 'strength' to the stimulus as measured by weight of sugar. But we have first to distinguish between the three pairs of terms given above.

Tone or *colour* is the popular or scientific or artistic name by which different kinds of light are distinguished—red, green, violet, &c. The wave-length of a homogeneous colour defines its position in the spectrum. The wave-lengths of the spectral colours range from $\frac{700}{1000000}$ at the red end to $\frac{400}{1000000}$ at the violet end; at about the middle of the spectrum (green-blue) the wave-length is $\frac{500}{1000000}$ or $\frac{1}{2}\ \mu$. Mixture tones may be recognised as such and their components identified by submitting them to the test of a prism—*e.g.* a homogeneous orange remains orange; a mixture orange, indistinguishable from it by the naked eye, exhibits the red and yellow when viewed through a prism. *Saturation or fulness* is to be carefully distinguished from brightness or strength; it depends upon the amount of white light with which the colour may be mixed; a colour is full or saturated when it is free from white light, pale or unsaturated when it is mixed with much white light. *Brightness* or *strength* of colour depends upon the strength of the white light from which it is derived; a colour is dark or bright according as there is much or little of it.

It is desirable to recognise the terms in common use which it is correct or not correct to use in opposition to each other. It is not correct to use pale and dark as opposed terms, nor even light and dark as applied to colour; the accurate terms to use are 'pale' or 'light' *versus* 'full' as regards saturation, 'dark' *versus* 'bright' as regards strength. Pale or light red is a dilute red in much white, dark red is a weak red derived from a small quantity of white light. And the same for other colours, the common names of which may be grouped as follows:—

Pale or 'dilute'	Normal	Dark or 'weak'
Rose or Flesh	Red	Maroon
Straw	Yellow	Brown
Light green	Green	Olive
Light blue	Blue	Dark blue

The distinction between saturation and brightness is very well illustrated by contrasting the effects of one of Maxwell's colour discs—say red—in combination with a white disc, and in combination with a black disc. In the first case the red is diluted with white, and a pale or light or less saturated red is the effect; in the second case the amount of red is reduced, and a dark red is the result. We may give one more example of the distinction. A red surface illuminated by white light may be said to reflect red rays and to absorb all others. A highly saturated red surface illuminated by a strong white light is 'bright' red; if faintly illuminated it is 'dark' red. An unsaturated red surface illuminated by white light is 'light' or 'pale' red.

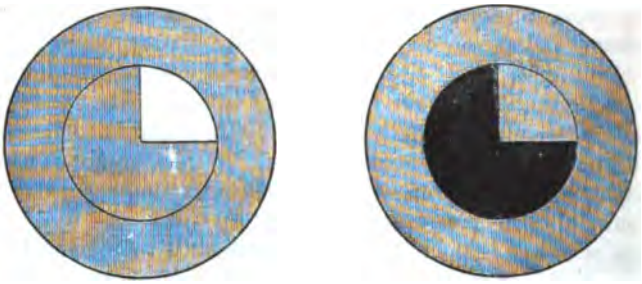


FIG. 197.—MAXWELL'S DISCS.

Arranged to illustrate difference of saturation and difference of brightness. In each case the outer circle is red; in the left-hand disc, the central part is three-parts red to one part white, and when rapidly revolved appears *pale red*; in the right-hand disc, the central part is one part red to four parts black, and when rapidly revolved appears *dark red.*

The distinction which we alluded to above as being desirable between brightness and strength, although not easy nor even possible to observe strictly, serves, however, to call attention to a distinction which is of the greatest importance, viz. that between sensory comparisons and stimulation measurements. We shall find in a later section (p. 536) that the ratio between these two variants is not arithmetical but geometrical, and that our measure of sensation is an indirect one by a varying unit. Differences of 'tone,' of 'brightness,' and of 'saturation,' are discriminated in sensation; these names are therefore applicable to the subjective aspect of colour differences. Wave-length, and in less degree saturation, are quantities accessible to instrumental measurements; these terms are therefore applicable to the objective aspect of colour differences. But we can draw no hard and fast line in the terminology; the strength of a stimulus is measurable, but we often speak of the strength of a sensation which can be expressed only in ratios and not in fixed units. Saturation is indiscriminately applied to the objective and to the subjective aspect of colour quantity. Physically all the spectral colours are saturated; physiologically some spectral colours are more saturated than others. A physically saturated colour is a maximum value which may be represented by a fixed number, the sensation to which it gives rise is its physiological maximum effect, but the latter is not a constant, and cannot be represented by a fixed number; the fixed maximum stimulus of spectral red will give rise to a smaller physiological maximum by an eye which is fatigued by red, and to a larger physiological maximum by an eye which is fatigued by the complementary green-blue. We shall not pursue these considerations further, having said enough to remind the reader that the subjective factor is variable, and that it plays a large part in the estimation of colour quantities—necessarily so, since the instrument by which we can measure and compare differences of that form of radiant energy called light, or colour, is the retino-cerebral apparatus by which we feel them.

Absorption of light.—Opaque bodies arrest the passage of all light; transparent bodies like glass or water allow light to pass unchanged, provided they are themselves colourless. But coloured transparent bodies stop the light of certain parts of the spectrum, while they allow that of other parts to pass. Thus red, yellow, blue, or otherwise coloured glass allow only red, yellow, blue, or other coloured light to pass, the remainder of the spectrum being in each case stopped by absorption. That this is really the case—*i.e.* that the light which passes through a red glass is white light *minus* orange, yellow, green, blue and violet, and not white light *plus* red light—may easily be verified by looking at the spectrum of white light passed through a red glass; only the red end of the spectrum remains visible, the light on the violet side of the D line is stopped, or as it were 'filtered off,' by the red glass.

The colours of bodies viewed by reflected light are likewise due to absorption. Red velvet illuminated by white light absorbs all except red light, which it reflects to the eye.

It is not always possible to tell by inspection of a coloured body what will be the precise portions of the spectrum which will be absorbed by it; in the familiar instance of blood, for example, the absorption bands revealed by the spectroscope are such as could not have been foreseen from the colour of diluted blood, and are so peculiar as to afford a delicate means of identification. The same example may be utilised to show that the absorption which takes place with reflected light is identical with that which takes place with transmitted light; if a little blood be smeared over a piece of white paper, and looked *at* with a spectroscope in a strong light, the absorption bands are seen just as if a layer of blood were looked *through* in the ordinary way. The last instance is indeed such as to indicate to us that the absorption of reflected light is essentially the same as that of transmitted light, inasmuch as the coloured reflected light is actually transmitted *through* a superficial film of the body which is looked at.

Retinal fusion of colours.—1. A vertical plate of glass placed between two horizontal coloured surfaces—*e.g.* blue and yellow—reflects one colour, while the second colour is seen through the glass. The two colours are thus simultaneously viewed together, and their resultant in sensation is a single effect approximating to white.

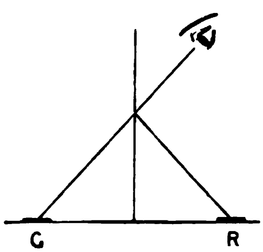


FIG. 198.

2. A rapidly rotating disc upon which sectors of any two or more colours are fixed, gives in sensation a resultant which is a single compound colour. Each colour is viewed in rapid succession, and, owing to the persistence of retinal impressions, the two or more constituent colour impressions cover each other and blend, giving a single compound colour. This is the method alluded to above as that by Maxwell's discs.

3. Two separate prismatic spectra are superposed so that various colours coincide. With suitable apparatus this method is by far the best; the separate colours are the purest possible, and the resultants from their mixture are correspondingly pure. The first two methods are only suitable for demonstration, for colours painted upon a surface are necessarily impure.

Physiological theories.—Most of the facts relating to colour-vision, its defects, and various experimental modifications, may be accounted for in accordance with a theory known as the *Young-Helmholtz Theory.* It is as follows: the cones of the retina, or the nerve-fibres connected with them, are of three different kinds as regards their excitability by various colours of light; one kind of cones is most excitable by red rays, less excitable by green and violet rays; a second kind is most excitable by green rays, less excitable by red and violet rays; a third kind is most excitable by violet rays, less excitable by red and green rays. This supposition is represented by the three curves R, G, V in fig. 199.

This theory is to be regarded more as a convenient standard to which various facts may be referred, rather than as itself a material demonstrated fact. It should not be employed as an explanation of facts, but only as a convenient supposition upon which certain facts may provisionally be placed together.[1] That the theory is not an actual expression of fact is clearly indicated by the following experiment:—A spot of white light forming on the retina an image less than 2 μ in diameter, does not assume any colour if cast upon various points, effects of chromatic dispersion being excluded; a minute spot of homogeneous colour does not alter under similar conditions; on the contrary, colour differences are more and more difficult to distinguish the smaller the area from which they proceed, and if exceedingly minute are no longer distinguished at all, but seen simply as colourless light.

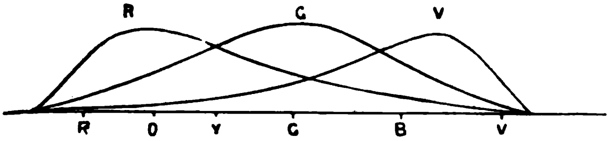


FIG. 199.

The alternative theory is that of Hering. The visual apparatus is supposed to be capable of six fundamental distinct sensations—white and black, red and green, yellow and blue. White, red, and yellow sensations are katabolic—*i.e.*, are concomitants of disintegration; black, green, and blue are anabolic—*i.e.*, concomitants of integration. The visual substance is further supposed to be of three kinds; changes of the first give white or black, of the second red or green, of the third yellow or blue. The white-black substance is supposed to be influenced by the whole range of the spectrum; the red-green to be used by red rays, restored by green rays; the yellow-blue to be used by yellow rays, restored by blue rays.

Colour-blindness.—A considerable percentage of people (5 per cent.) fail to distinguish colours from each other which to the majority of people are perfectly different. When this inability is very marked, its subject is said to be colour-blind. Colour-blindness varies in degree and character, but by far the commonest form is that in which the discrimination of red from green is imperfect. This defect has very obvious practical importance as regards railway and steamship officials, who should be able to distinguish without hesitation between green and red lights. The assured fact that a given person confuses red and green—*i.e.* that red and green rays excite the same kind of sensation—is attributed to the by no means assured fact that cones most excitable by red rays are not present in his retinæ (Helmholtz), or that the red-green visual substance is wanting (Hering).

---

[1] The purely imaginary nature of this hypothesis is insisted upon by Helmholtz himself, who in the 2nd edition of his *Physiological Optics* (1889, p. 349) supplements it by the assumption of three kinds of photochemically changeable substances, and of three kinds of cells in the cerebral cortex.

The colour-perimeter.—If, while the eye is fixed upon a point directly in front of it, the extent of the field of indirect vision be tested, by moving a small disc so as to come in and out of the field from several sides, it will be found that the extent of the field of indirect vision is greatest for a white disc, smallest for a red disc, and that the field is greater for green than for red, and greater for blue than for green. (See also p. 420.)

VISION

The organ of vision is composed of (1) a *receptive* part—the eye; (2) a *transmissive* part—the optic nerve; and (3) a *perceptive* part—the cortex of the brain over the occipital lobes.

The eye is essentially a *camera obscura*, having anteriorly a *biconvex lens* by which images of external objects are focussed upon a sensitive surface, *the retina.* Muscles attached to the eyeball turn the eye in various directions towards various points of the field of vision. The exact focussing of images formed by objects near to and far from the eye is affected by alterations of the focussing power of the lens, and not, as in the photographic camera, by alterations of the distance between lens and sensitive surface. The focussing power of the lens is altered by the action of the ciliary muscle—this change constituting the act of accommodation. A circular diaphragm—the iris—cuts off light from all but the central part of the lens, and contracts or dilates by muscular action under a variety of conditions.

The eye is almost spherical, the greater part of its wall is composed of three coats—the sclerotic, choroid, and retina. The posterior $\frac{5}{6}$ of the wall are opaque, the anterior $\frac{1}{6}$ of the wall is transparent and is named the cornea; it is continuous with the sclerotic. The iris is continuous with the choroid, both usually are deeply pigmented and effectually convert the interior of the eye into a dark chamber; the pupil, or central aperture of the iris, is made smaller or larger by the contraction of circular muscular fibres in the iris (constrictors) or of radiating muscular fibres (dilatators). The circular or constrictor fibres are excited to contraction through the channel of the third or motor oculi nerve; the radiating or dilatator fibres are excited to contraction through the channel of the cervical sympathetic. The retina is the expansion of the optic nerve as the internal of the three coats; it occupies the posterior $\frac{2}{3}$ of the internal surface; and is composed of several layers; the most external of these layers—

the layer of rods and cones—is excitable by light and is the true end-organ of the optic nerve; it is, like all other sensificatory surfaces, composed of elements which are modified epithelial cells, originally derived from the external epithelium of the embryo (the epiblast). The contents of the eyeball are (1) the aqueous humour in the anterior chamber, (2) the crystalline lens held in place by its capsule and suspensory ligament, to which is attached the ciliary muscle, (3) the vitreous body. These three substances are transparent, and with the cornea constitute the refractive media of the eye, which conjointly act as a converging lens.

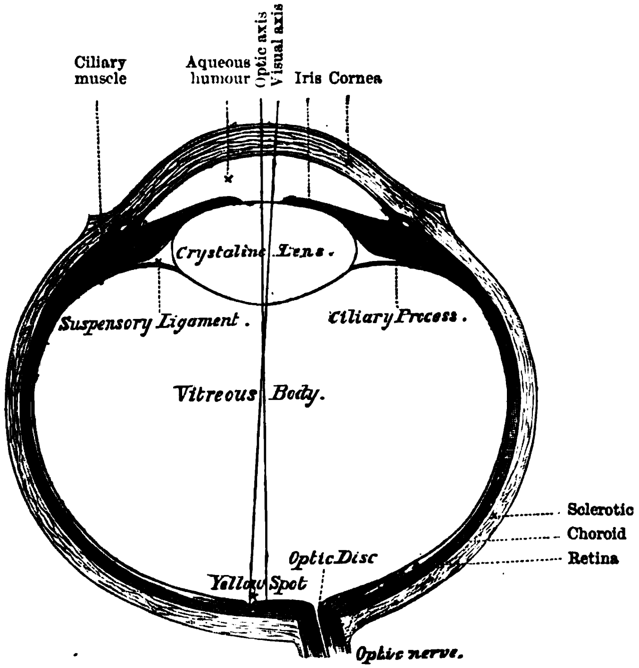


FIG. 200.—HORIZONTAL SECTION OF THE LEFT EYEBALL.

The retina is a comparatively thick stratified membrane, comprising from vitreous to choroid surface the series of layers shown in fig. 201.

The essential terminal apparatus is constituted by the rods and cones of the seventh layer, which is contiguous with the choroid, and not, as might have been imagined, the superficial layer first exposed to the impact of light. A ray of light must traverse the layers in the direction from 1 to 7 before it gives rise to a nervous impulse at the second layer; this impulse travels through the layers in the reverse direction from 7 to 1, and is led off by the fibres (non-medullated) of this layer, which converge to form the optic nerve, where they become medullated. The retinal blood-supply is derived from the central artery, which branches out from the optic disc and forms a superficial ramification, the capillaries from which are confined to the first four layers of the retina; the remaining layers are therefore extravascular; and it is to be noticed that the vessels are thus situated on the path of light in front of the layer of rods and cones, so that it is possible for shadows of the vessels to be cast upon this layer.

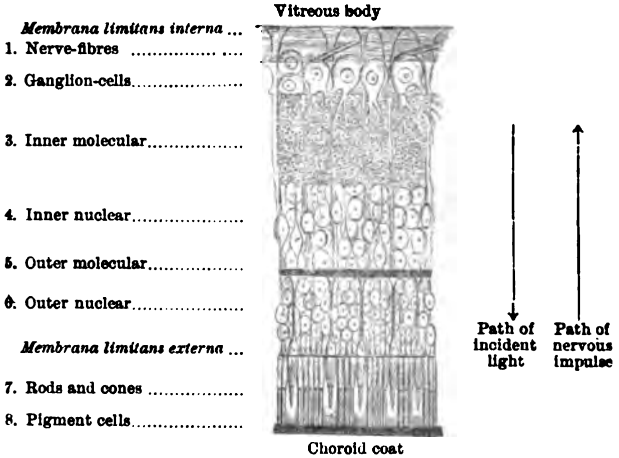

Vitreous body
Membrana limitans interna ...
1. Nerve-fibres ....
2. Ganglion-cells....................
3. Inner molecular.................
4. Inner nuclear.....................
5. Outer molecular..................
6. Outer nuclear.....................
Membrana limitans externa ...
7. Rods and cones ....
8. Pigment cells.....................
Path of incident light
Path of nervous impulse
Choroid coat

FIG. 201.—THE RETINA.

The elements composing these several layers are held together and supported by 'sustentacular' connective-tissue, which supports the nervous elements proper and forms membranous sheets—the external and internal limiting membranes—between which are included the inner first six layers of the retina.

The structure of the retina differs from that indicated above at two exceptional points, viz. at the optic disc and at the yellow spot. The optic disc is the point at which the optic nerve enters the eyeball, and whence its fibres spread out in all directions over the inner surface of the eyeball. This spot is destitute of true retina and is not excitable by light; its situation and dimensions can be experimentally determined by Mariotte's experiment. At the yellow spot, or more precisely at the fovea centralis, or central depression in the middle of the yellow spot, the retina is very thin, consisting of little more than a single layer of attenuated cones. It is the region of most distinct vision—*i.e.* the spot upon which objects are imaged when they are looked at; but *not* the area of the greatest sensibility—on the contrary. These anatomical points taken in conjunction with the experiments of Mariotte (p. 413) and of Purkinje (p. 438) constitute proof positive that the rod and cone layer of the retina is the layer excitable by light and excitatory of visual sensation.

It is to be remembered that the eye as a converging lens differs from an ordinary biconvex lens in this respect, that the rays are twice refracted at the surfaces of the latter—once at entrance from air, once at exit into air—whereas in the eye the chief refraction occurs at the entrance surface from air, namely at the cornea, subsequent refraction by the other media being of comparatively small amount. Of these subsequent media, the crystalline lens is certainly the most important, as by it is obtained the additional refractive power required in accommodation; but that the lens is not absolutely essential to vision is clearly shown by the condition of sight after it has been extracted for cataract; accommodation is then lost, and the eye is hypermetropic by the loss of about 10 diopters lens power, but the patient obtains a useful eye. The power of such an eye requires to be supplemented by a 10 diopter glass for distant vision, and for vision at a distance of 20 centimeters by a 15 diopter glass.

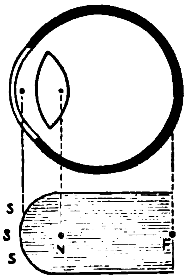


FIG. 202.—THE REDUCED OR SCHEMATIC EYE.

Radius of curvature of refracting surface S S S = 5 mm.
Index of refraction . . = 1·35
Position of nodal point N . . . . = 5 mm behind S S S.
Position of principal focus F . . . = 15 behind N. or 20 mm. behind S S S.

Such an eye would be approximately represented by a piece of glass shaped like the lower figure.

The various refractive media (of which the list on p. 424 gives the normal values) may, as regards their total converging effect, be considered equivalent to that of a single substance with a refractive index of 1·35, and a single spherical surface of 5·1248 mm. radius. In such a medium the distance between the nodal point N and the principal focus F is about 15 mm. Its collecting power is equal to about 50 diopters—*i.e.* it is a convex lens with a focal distance of 2 cm. This is a schematic or *reduced eye*. Taking the retina as the point of departure, the nodal point N of such a reduced eye, as compared with the normal eye, will be just in front of the posterior surface of the lens, and the one refracting surface will be midway between the anterior surface of the lens and the posterior surface of the cornea.

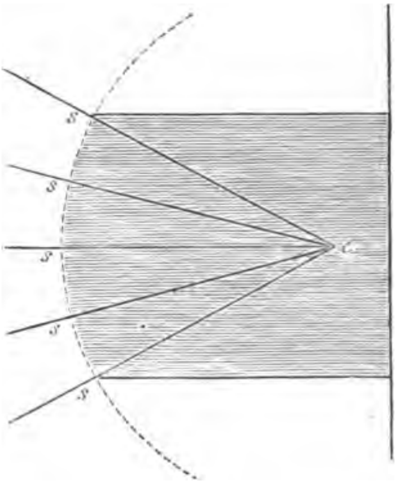


FIG. 203.

s s s s s is the spherical surface of a mass of glass; *c* is the centre of curvature of that surface. The radii, *c s*, are perpendicular to the surface, and rays of light entering the glass on these lines will not be deflected, but will meet at the point *c*. Lines of this kind (viz. perpendicular to the surface of separation) are termed '*lines of direction*,' and *c*, their point of intersection, is termed the '*nodal point*.' In other words, the nodal point may be defined as the point of intersection of rays perpendicular to the refracting surface. In the case of the eye there are several such nodal points behind its several refractive surfaces. But in the schematic eye described above we have considered these surfaces and points as represented by one surface and one nodal point.

The *optic axis* is a straight line through the centres of curvature of the cornea and lens, prolonged to the posterior wall of the eye; the point at which the optic axis meets the retina is between the fovea and the entrance of the optic nerve.

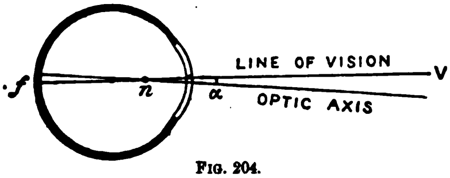


FIG. 204.

The *line of vision* may be defined as a straight line, *f* V, between the fovea and any point to which the gaze is directed. It does not coincide with the optic axis, but forms with it an angle of about five degrees (fig. 204). It may also be defined as the prolongation forwards of a straight line from the fovea to the nodal point (of the reduced eye).

Visual angle.—The angle B *n* A included between two straight lines from the borders of an object B A to the nodal point *n* is called the visual angle; it is equal to the opposite angle *b n a*.

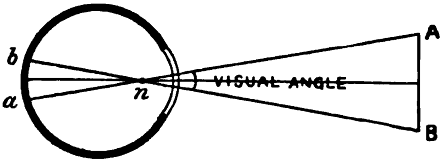


FIG. 205.

The value of the distance N F (fig. 202 :15 mm. in the normal eye) supplies a necessary datum in calculating the size of the retinal image of an object—given the size of the object, and its distance from the eye.

For example, what will be the height on the retina of an observer, of a man six feet high at a distance of one mile ?

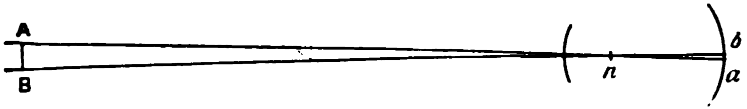


FIG. 206.

Let A B represent the man, *a b* the image of the man on the eye of an observer, *n* being the nodal point of that eye.

From the two similar triangles A *n* B, *a n b*, we have $\frac{a\,b}{a n}=\frac{\mathrm{A\,B}}{\mathrm{A}\,n}$ or, substituting the numbers given above, $\frac{a\,b}{15\text{ mm.}}=\frac{6\text{ feet}}{1\text{ mile}}$; that is, $a\,b$ $=0{\cdot}017$ mm., *i.e.* 17 μ.

This is about twice the diameter of a blood-corpuscle. We know that a man will be visible at a much greater distance than one mile—*i.e.* when forming on the eye a retinal image much smaller than 17 μ—a consideration which brings home to the mind that it is under certain conditions possible to see blood-corpuscles in one's own retina.

Another good example of the application of the reduced eye, especially as regards the magnitude N F=15 mm., is afforded by the following exercise :—Determine on your own eye the distance between the yellow spot and the entrance of the optic nerve—*i.e.* the blind spot (Mariotte's experiment). The problem can easily be solved as follows:—Pin a large sheet of white paper against the wall, mark on it a small black cross, C, on a level with the eyes, steadily look with one eye at the cross, having fixed the position of the head by a ruler of convenient length (say 50 cm.) held between the teeth and resting against the wall; while the gaze is thus fixed move a white quill pen with inked point towards the temporal side of the field of vision, and mark on the paper the exact spot at which the black point is lost sight of.

Under the above conditions the retinal image of the cross is on the centre of the yellow spot, and the second mark shows where the image of the black mark has passed over the temporal border of the blind spot.

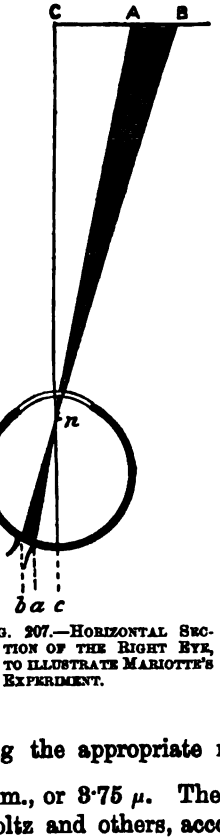


FIG. 207.—HORIZONTAL SECTION OF THE RIGHT EYE, TO ILLUSTRATE MARIOTTE'S EXPERIMENT.

In the experiment just made the distance between the two points A and C was 10 cm., that from *n* to C was 50 cm.; therefore, $\frac{10}{50}=\frac{ac}{15}$; that is, *a c*, the distance between the centre of the yellow spot and the temporal border of the optic disc, = 3 mm.

Similarly by moving the black-tipped pen in various directions we may determine the limits of the blind field, and from its magnitude A B deduce the retinal magnitude of the blind spot *a b*. In the above example the horizontal magnitude, A B, was 6 cm.—*i.e.* the retinal magnitude was 1·8 mm.; measured vertically, the diameter of the blind field was 8 cm.—*i.e.* its retinal magnitude was 2·4 mm.

To determine the smallest perceptible image on the retina.—Gum two slips of white paper 1 mm. wide parallel with each other on a black card, leaving an interval 1 mm. broad between the two slips. Determine the distance from the eye at which the two white slips are just visible, or just invisible as a *double* line. In the observation just taken the distance was about 4 meters.

As before $\frac{ab}{an}=\frac{AB}{An}$ (fig. 206), or substituting the appropriate numbers $\frac{ab}{15\text{ mm.}}=\frac{1\text{ mm.}}{4000\text{ mm.}}$ *i.e.* $ab = \cdot 00375$ mm., or 3·75 μ. The result agrees with the classical results of Helmholtz and others, according to which the smallest angular distance at which points can be separately distinguished is 50 sec., with which the size of a retinal image is 3·65 μ. It is to be observed that this magnitude closely coincides with the diameter of cones at the fovea, which is about 3 μ, the distance between the centres of adjacent cones being about 4 μ.

Accommodation.—The formation of a distinct image upon the retina is necessary to distinct vision. With any given lens distinct images of different objects near or far, may be obtained by altering the distance between the lens and the surface upon which the image is to be formed; if this distance is unalterable, a more or less convergent lens must be used for near and for distant objects respectively. In the case of the eye the distance between the lens and the retina is invariable, but the lens may be rendered more or less convex by more or less muscular action. The lens is lodged between two layers of the suspensory ligament, which is a prolongation of the choroid, and is kept compressed by the tension of that membrane; a circular muscle, the *ciliary muscle*, having its fixed point at the junction of the cornea and sclerotic, and its insertion in the choroid, can pull upon the choroid so as to relax the tension of the suspensory ligament, when the lens by virtue of its elasticity becomes more convex. A more convex lens is a more convergent lens, and has a shorter focus—*i.e.* divergent rays from a near object which in a resting eye with compressed lens would be focussed behind the retina, are now brought to a focus on the retina itself, and the object is seen distinctly. The change thus effected by the agency of the ciliary muscle, constitutes the act of *accommodation*, which is a voluntary act (although the ciliary muscle is composed of smooth fibre). With relaxed accommodation the eye is adjusted to distinct vision of distant objects, the rays from these to the eye are practically parallel, the suspensory ligament is tense, the lens is compressed, the ciliary muscle is at rest. With accommodation the eye is adjusted to distinct vision of near objects, the rays from these to the eye are divergent, the suspensory ligament is less tense, the lens is less compressed, the ciliary muscle is in action. With the normal eye distant objects are seen without accommodation, the converging power of the lens and the length of the eye are such that distinct images are formed on the retina, of objects from which the rays to the eye are parallel. Accommodation is only required for near objects, and in the normal eye the power of accommodation is such as to procure distinct images of objects up to about 5 inches from the eye; within this distance distinct images can no longer be obtained. The most distant point of which distinct vision is

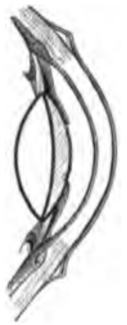


FIG. 208.

To illustrate accommodation: non-accommodated compressed lens represented clear; additional curvtaure by the bulging of its anterior surface in extreme accommodation represented by the shaded crescent.

possible is called the 'far point'; the nearest point of which distinct vision is possible is called the 'near point'; in the normal eye of a person 30 years old the far point is at an infinite distance, the near point is at about 5 inches from the eye.

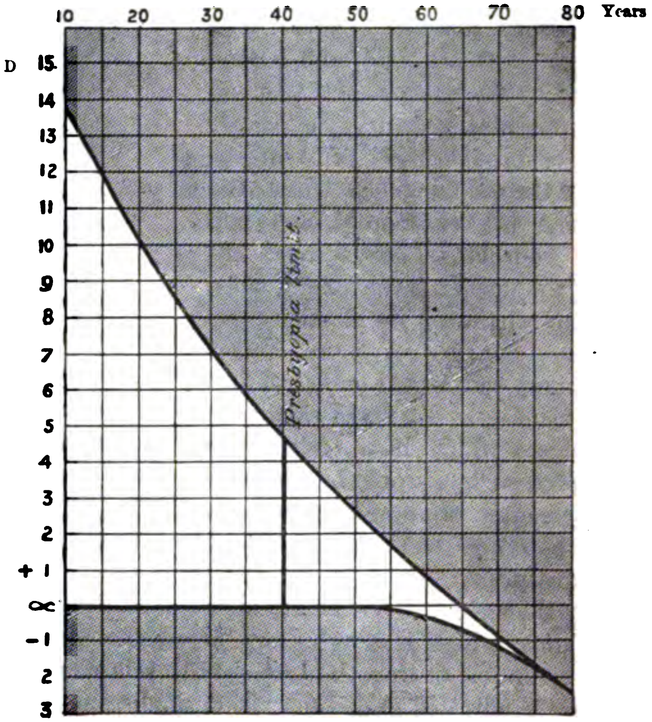


FIG. 209.—POWER OF ACCOMMODATION AT DIFFERENT AGES.

The ordinates indicate power in diopters. Age is indicated by the numbers along the abscissa—*e.g.* at 20 years the range is between infinity for the resting eye and 10 diopters for the accommodated eye; at 30 years the range is from infinity to 7 diopters; soon after 50 years, the resting eye is under-focussed for infinity; soon after 65 years, even a fully accommodated eye is under-focussed for infinity. The focussing power must be supplemented by convex glasses, increasing in strength with increasing age. (Donders.)

Myopia.—The vision of distant objects is indistinct, and objects can be distinctly seen nearer than usual—the subject is said to be 'short-sighted.' The defect is due to the fact that the converging power is too great in relation to the length of the eye, or, more correctly, that the eye is too long in relation to its converging power; parallel rays are focussed in front of the retina, and even very divergent rays can be focussed on the retina. A scattering or biconcave lens is the corrective of this too great converging effect.

Hypermetropia and presbyopia.—Near objects cannot be distinctly seen, distant objects may be clearly seen. The subject is said to be 'long-sighted.' The eye is not long enough in relation to its converging power; divergent rays cannot be focussed on the retina, but have their focus behind it; parallel rays may be brought to a focus on the retina unless the affection be excessive. The hypermetropic eye is shorter than the normal

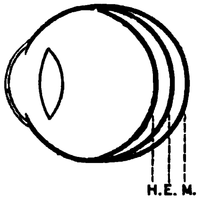


FIG 211.

H. *Hypermetropia.* — Short eye. Long sight.
E. *Emmetropia.* — Normal eye. Normal sight.
M. *Myopia.* — Long eye. Short sight.

The figure represents high degrees of hypermetropia and of myopia, *i.e.* an alteration in each case of about 12 diopters. The normal eye being 22 mm. long, the short eye will then be about 18 mm, and the long eye about 26 mm in length.

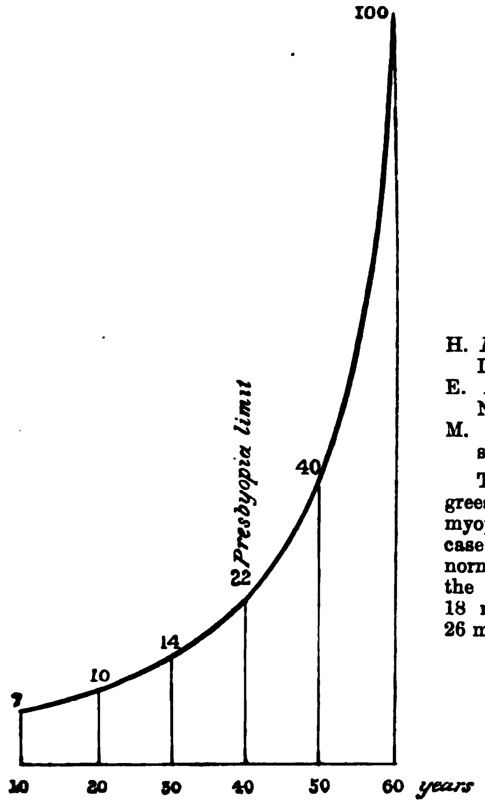
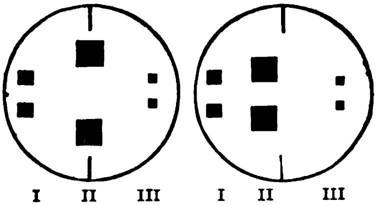


FIG. 210.—RECESSION OF PUNCTUM PROXIMUM WITH INCREASING AGE.

The ordinates in millimeters indicate the distance of the 'near point' in centimeters. When the 'near point' is further than 22 cm. presbyopia is said to begin. Normally this occurs at the age of 40. In more or less myopic eyes, the 'near point' is at about 10 cm., the 'far point' at 30 to 50 cm. The 'far point' of the normal eye is at infinity.

eye, an effort of accommodation is requisite even to distant distinct vision, and if the hypermetropia be excessive, even this is insufficient to effect focussing upon the retina. The *presbyopic* eye has a rigid lens or a weak ciliary muscle, so that the lens cannot become convex when accommodation is attempted. A gathering or biconvex lens is the corrective of these deficient converging effects both in hypermetropia and in presbyopia.

Sanson's images.—That it is the lens and lens only that is altered in the act of accommodation is proved by the observation of 'Sanson's images.' A candle held in an appropriate position close to an eye, gives three reflections, which can be seen by an observer placing himself at an appropriate angle, or more conveniently with the aid of the instrument known as the '*phakoscope.*' These are reflections from the mirror surfaces:—1, of the cornea; 2, of the anterior surface of the lens; 3, of the posterior surface of the lens. The first image is very bright and unmistakable; it is a reflection from the convex surface of the cornea, and is therefore an erect virtual image. The second image is larger and much less distinct, it is a reflection from the convex anterior surface of the lens; this surface is less convex than that of the cornea, and the image is erect, and larger than the corneal image. The third image is intermediate in distinctness between the first two and very small; it is a reflection from the concave posterior surface of the lens, and is therefore a real reversed image. If, while the observer has in view these three images (or, better still, three pairs of images from a double light) the subject of observation alternately relaxes and accommodates (*i.e.* looks alternately far and near in one line of vision), it may be seen that images I and III remain immobile and unchanged, but that image II advances towards image I and becomes smaller with the act of accommodation, that it recedes again from I and recovers size with relaxed accommodation. The stability of images I and III in the act of accommodation, proves that the cornea and posterior surface



With relaxed accommodation

With accommodation

FIG. 212.—SANSON'S IMAGES.

I. From surface of cornea. II. From anterior surface of lens. III. From posterior surface of lens.

of the lens do not move nor alter their curvature; the diminution in size and advance of image II prove that the anterior surface of the lens becomes more convex and approaches the cornea.[1] This testimony is proof that the act of accommodation is accompanied by increasing convexity of the anterior surface of the lens, and of the anterior surface of the lens only.

The fact may be observed, but not so accurately, by directing a person to look near and far along one line of vision, while his eye is looked at from the side so that the black border of the pupil is just visible. The iris may be seen to be pushed forwards with the act of accommodation. This is, of course, only a rough and partial observation of the fact, which is proved with great nicety by means of the three images.

In the course of these observations it will hardly have escaped notice that the pupil is larger when the eye is adjusted for distant vision, smaller when the eye is accommodated to near vision—*i.e. contraction of the pupil* accompanies the act of accommodation.

The *field of vision* is the entire surface from which rays of light reach the retina; in other words it is the total visible area in front of the open eye. The term is somewhat loosely applied with reference to the moving or to the stationary eye; strictly speaking, it applies to the latter only, and alters with every movement of the eye, its centre being always the particular spot from which rays are focussed upon the fovea centralis. This spot or point of fixation is the centre of a small area of distinct vision, which again is surrounded by a much larger area of indistinct vision. The area of distinct vision is included by an angle of about 1° only (the diameter of the fovea being only ¼ mm. the diameter of the distinct area in the field of vision at a distance of 30 centimeters will be only ½ centimeter, at a distance of 30 meters only ½ meter), while that of indistinct vision is for each eye about 160° horizontally, and 120° vertically; with both eyes open the horizontal range is over 180°.

To *look at* an object means to turn the eye in such a position and to accommodate its focussing power to such an extent, that a well-defined image of the object falls on the fovea; we then have distinct or 'direct vision of the object, and at the same time indistinct or 'indirect' vision of neighbouring objects which form more or less well-defined images on the retina further and further from the yellow spot. The retinal image is thus 'like a picture minutely and elaborately finished in the centre, but only roughly sketched in at the borders.' An apparent imperfection, but in reality an advantage to concentration of attention, since by the rapidity and exactness with which the eye can be turned from point to point, we can at will focus and minutely examine any spot; any such spot becomes the centre of the picture and a focus of attention, as well as a focus of vision.

---

[1] Image III does alter a little, but not enough to sensibly invalidate the statement made above.

The extent of the field of vision in any given case is measured by the *perimeter*, which is in principle a hemisphere, the centre of which serves as a point of fixation to the eye under examination (the other eye being closed), while the examiner determines on the hollow surface of the hemisphere those points at which the patient just ceases or just commences to see a small object moved in various directions. The observations plotted on skeleton charts, graduated in degrees, give in graphic form the field of vision of the stationary eye.

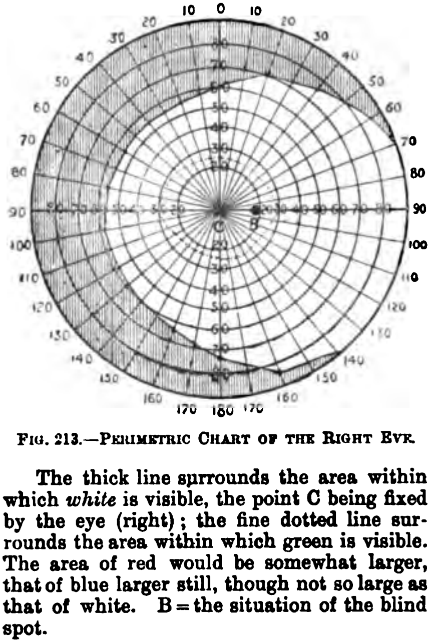


Fig. 213.—Perimetric Chart of the Right Eye.

The thick line surrounds the area within which *white* is visible, the point C being fixed by the eye (right); the fine dotted line surrounds the area within which green is visible. The area of red would be somewhat larger, that of blue larger still, though not so large as that of white. B = the situation of the blind spot.

Scheiner's experiment is deserving of careful repetition by anyone who desires to realise from a different point of view facts relating to accommodation, and in addition to this the formation of double images in a single eye, and the relation of retinal impressions to cerebral perceptions.

Two pin-holes are pricked in a card at about one millimeter from each other; and the card being held in front of one eye, with the two pin-holes side by side in front of the pupil, a needle, held vertically, is looked at through the holes.

1. With the eye accommodated for the needle, the latter is seen single, and if it be brought gradually nearer to the eye a point is reached at which it can no longer be seen single by any effort of accommodation; the distance of the needle in front of the eye is now that of the near point of distinct vision. With the eye accommodated

to a point either nearer or farther than the needle, the latter is seen double.

2. If the eye is accommodated to a point beyond the needle, or, better still, if it is non-accommodated, two images will appear; these will move towards each other as the needle is moved from the eye, will move away from each other as the needle is moved towards the eye. If the right-hand hole is covered, the apparent left-hand needle will disappear, and, *vice versâ*, if the left-hand hole is blocked the apparent right-hand needle will be lost.

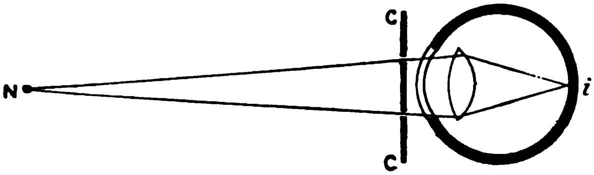


Fig. 214.—To illustrate Scheiner's Experiment.

N, Section of needle held horizontally. C C, Card pierced by two pin-holes one above the other held vertically. Vertical section of eyeball.

The eye is accommodated for the needle.

A single image is formed on the fovea, the needle is seen single.

The minimum distance at which the needle can still be seen single is the 'near point' of distinct vision.

3. If while the eye is accommodated to a point nearer than the needle, the latter be moved away from the eye, the two images will move away from each other; they will move towards each other as the needle is brought closer to the eye. Blocking the right-hand hole effaces the apparent right-hand needle, blocking the left-hand hole effaces the apparent left-hand needle.

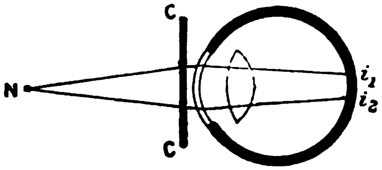


Fig. 215.—To illustrate Scheiner's Experiment.

The eye is accommodated *beyond* the needle or non-accommodated. It is therefore under-accommodated as regards the needle, which gives two images i_1 i_2 and therefore seen double.

If the needle is brought nearer to the eye the images enlarge and move away from each other; if it is moved further from the eye, the images become smaller and approach each other.

Blocking the upper hole in the card abolishes the retinal image i_1, i.e. the apparent inferior needle in the field of vision; blocking the lower hole abolishes i_2, i.e. the apparent superior needle.

The whole series of observations may be repeated with the needle held horizontally, the card being held so that the holes are one above the other in front of the pupil.

The lens of the eye, in common with other lenses, refracts blue rays more strongly than red rays. Consequently the focus of blue is nearer to the lens than the focus of red. A spot of white light is surrounded by a blue halo if the eye is focussed to a point beyond the spot, by a red halo if it is focussed to a point nearer than the spot; to see these halos distinctly the light should be viewed through cobalt glass, so as to cut off the yellow and green, allowing only red and blue to pass. A blue light and a red light at the same distance from the eye appear to be unequally distant; the red light requiring greater accommodation than the blue appears to be the nearer of the two, nor can both lights be exactly focussed together upon the retina. Of a red and a blue surface side by side, the red appears to be the nearer.[1] The difference is such that a normal eye focussed for parallel red rays is at the same time focussed for blue rays divergent from the points of a surface about three feet distant.

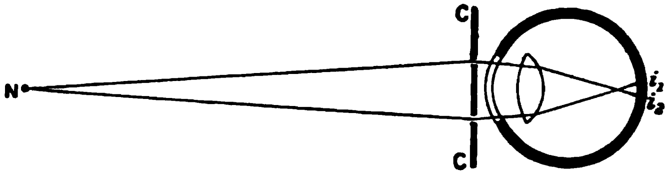


FIG. 216.—TO ILLUSTRATE SCHEINER'S EXPERIMENT.

The eye is accommodated to a point nearer than the needle. It is, therefore, over-accommodated as regards the needle, which gives two images, i_1 and i_2.

If the needle is brought closer the images enlarge and move towards each other; if it is moved further the images become smaller, and move away from each other.

Blocking the upper hole abolishes the retinal image i_2, i.e. the apparent superior needle; blocking the lower hole abolishes i_1, i.e. the apparent inferior needle.

Astigmatism.—The surface of the cornea is not perfectly spherical, the curvature of its vertical meridian is usually greater than that of its horizontal meridian, and the difference may be so pronounced as to interfere with the distinct focussing of objects. With a cornea of such curvatures ('spoon-shaped'), a point of light cannot form a focal point upon the retina (hence the name astigmatism), but forms a linear focus; if the eye is adjusted so that the rays diverging from the point in the vertical plane (meridian of greater curvature) come to a focus on the retina, then the rays diverging from the point in the horizontal plane (meridian of lesser curvature) will reach the retina before they have come to a focus (*i.e.* be under-focussed), and a horizontal linear focus will be formed; *vice versâ*, if the eye is adjusted so that rays in the horizontal plane (meridian of lesser curvature) are focussed upon the retina, then the rays in the vertical plane will reach the retina after coming to a focus (*i.e.* be over-focussed), and a vertical linear focus will be formed. As shown in the diagram the horizontal linear focus f_1 is nearer than the vertical linear focus f_2.

---

[1] This is not a complete explanation. Einthoven has shown that the effect is mainly dependent upon excentricity of the pupil. Most persons see red in front of blue, but some persons see blue in front of red.

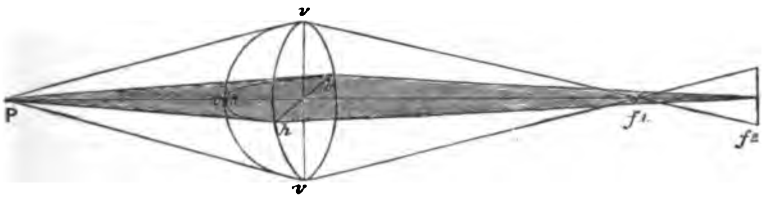


FIG. 217.—REGULAR ASTIGMATISM.

The curvature of the cornea is greater in the vertical meridian, *v v v*, than in the horizontal meridian, *h h h*. The point of light P consequently has a first linear focus at f_1 which is horizontal, and a second linear focus at f_2, which is vertical. If, instead of P, the object were a vertical and a horizontal line crossed, the vertical line would be in focus at f_2, the horizontal line would be in focus at f_1. To bring the two lines into focus at the same time on the same plane, it would be necessary to use a convex cylindrical glass to add to the horizontal convexity *h h h*, or a concave cylindrical glass to subtract from the vertical convexity *v v v*.

Consider next the case of a series of points, viz. a line, vertical or horizontal. A person whose cornea is regularly astigmatic, as supposed above, can see distinctly either a horizontal or a vertical line, but not both together. If the eye is focussed for a horizontal line it is under-focussed for a vertical line, if it is focussed for a vertical line it is over-focussed for a horizontal line; thus the astigmatic eye cannot be accurately focussed at one and the same time for a vertical and a horizontal line which cross each other, one or other must be indistinct (over- or under-focussed); a greater effort of accommodation being required to focus a vertical than a horizontal line, the former appears to be nearer to the observer than the latter—*i.e.* a vertical line appears to be in front of a horizontal line which it crosses in the same plane; further, as the eye has greater focussing power upon a horizontal than upon a vertical line, the former remains distinctly visible at a shorter distance from the eye than the latter.

Irradiation.—The media of the eye are not perfectly transparent, the lens is not perfectly homogeneous. These causes must also contribute to the slight defect of focussing present even in the most normal eye, and cause a certain amount of dispersion or 'irradiation.'

AVERAGE MEASUREMENTS OF THE NORMAL EYE

	mm.
Antero-posterior diameter of eyeball	24
Radius of curvature of cornea	8
„ „ ant. surface of lens (non-accom.)	10
„ „ „ „ (accom.)	6
Radius of curvature of posterior surface of lens	6
Refractive index of aqueous humour	1·34
„ „ vitreous humour	1·34
Mean refractive index of lens	1·45
Diameter of cornea	12
Distance between cornea and lens	4
Mean diameter of pupil	4
Thickness of cornea	1
„ lens (non-accommodated)	4
„ lens (accommodated)	4·4
Thickness of retina at fundus	0·2 to 0·3
Distance between retinal vessels and rod and cone layer	0·2 to 0·3
Diameter of optic disc	1·5
„ yellow spot	1·25
„ fovea centralis	0·25
„ cone in fovea	0·004 to 0·005

Relation of retina to field of vision.—In performing Scheiner's experiment the observer will have noticed that by blotting out the image which is superior, inferior, right or left as regards its retinal position, he loses sight of the apparent image in his field of vision which is inferior, superior, left or right. In other words, impressions made on the upper, lower, right or left part of the retina excite in consciousness the sensations that objects are situated below or above, to the left or to the right, of the line of vision. We may easily recognise this to be a necessary relation when we have realised that the retinal image is reversed, objects at our feet being focussed on the upper portion of the retina, objects above our heads on its lower portion, objects to our left on its right half, objects to our right on its left half. If, as sometimes occurs, the lateral halves of the two retinæ are paralysed, say on the right side (right hemiopia), the left half of the field of vision is blotted out (left hemianopia); *vice versâ*, left hemiopia

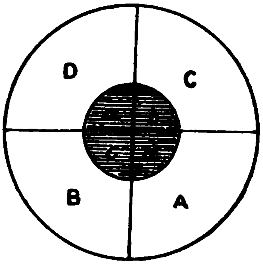


FIG. 218.

The quadrants A B C D of the field of vision are projected upon the quadrants *a b c d* of the retina.

of the two retinæ will cause right hemianopia as regards the field of vision.[1]

Moreover, we normally see objects single with both eyes open, although two retinal images are formed, one in each eye. This is due to the fact that when an object is looked at, its image (and those of its immediate surroundings) are focussed upon *corresponding parts* of the two retinæ. The doctrine of corresponding points will, however, be best understood by taking into account the circumstances under which, correspondence not being effected, double vision occurs. Before so doing it should be remarked that in Scheiner's experiment we have experienced double vision with only one eye open; this obviously being due to the fact that we have, by means of the two pin-holes, made two images of the same object fall upon different parts of the same retina.

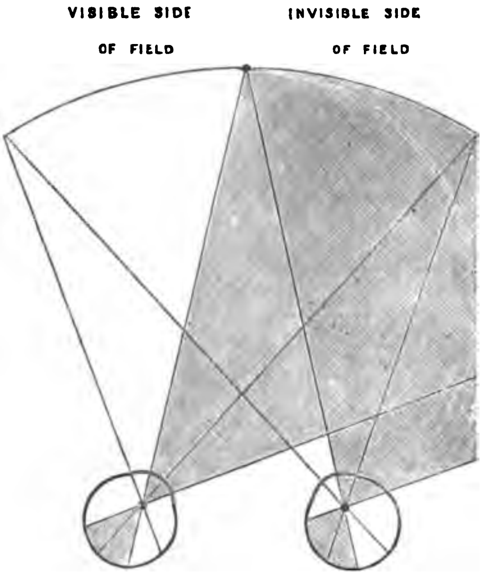


FIG. 219.—LEFT HEMIOPIA AND RIGHT HEMIANOPIA.

Corresponding points.—Single vision with the two eyes and double vision with the two eyes differ in this respect, that in the former the object gives on each side of the two retinæ an image, every point of which comes to a focus upon each of two corresponding points in the two retinæ, while in the latter the two retinal images are not outlined upon corresponding points. In the first case the excitations caused by the two corresponding images fuse in consciousness and cause perception of a single object; in the second the excitations of the two non-corresponding images do not so fuse, and the perception of an apparently double object is their consequence. Corresponding points are thus physiological pairs of points, one in the right eye, one in the left eye, from the simultaneous stimulation of which a single optical sensation results; anatomically they are almost exactly the symmetrical points in the two retinæ which would cover each other in pairs if the two retinæ were superposed one upon the other, with the yellow spots as centre.

---

[1] The unguarded use of these terms in various senses leads to much unnecessary confusion, and their meaning is sometimes only to be gathered from the context. Hemiopia is literally half-vision, while hemianopia (or hemianopsia) is half-blindness. The expression 'left hemiopia,' as used by different writers, may mean paralysis of the right or left halves of the retina, or blindness to the left or to the right of the subject. All ambiguity is removed by stating the sides to which vision is preserved or lost.

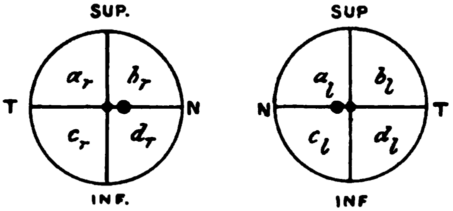


FIG. 220.

a_r b_r c_r d_r and a_l b_l c_l d_l, are corresponding quadrants in the two retinæ and would exactly cover each other if superposed. Each quadrant may similarly be imagined to be symmetrically divided into symmetrical corresponding parts, and each such part further subdivided into single rods and cones symmetrically situated in the two retinæ, *i.e.* corresponding.

The yellow spots correspond in the two eyes, and when an object is looked at, its image is formed upon each of the two yellow spots. The blind spots in the two eyes do not correspond; being situated in the nasal segment in each eye, they would not cover each other if the retinæ were superposed as above described. The nasal side of the left eye corresponds with the temporal side of the right eye, and the temporal side of the left eye with the nasal side of the right eye.

The horopter.—The horopter is that surface or series of points in space, the images of which fall upon corresponding points of the two retinæ. A complete exposition of the form assumed by the horopter with various positions of the eyeball would necessitate a mathematical analysis far beyond the scope of a simple text-book of physiology; we shall here restrict ourselves to the verbal definition of the 'horopter,' and to the geometrical definition of Müller's horopteric circle, which occurs when the visual axes converge upon a near object.

In this position the horopter is formed by a horizontal circle passing through the object, and through the nodal points of the two eyeballs, and by a straight line drawn through the point of fixation in the median plane tilted away from the observer. Müller's horopteric circle is a practical illustration of prop. 21 of Book III. of Euclid, in which it is demonstrated that any given chord of a circle sub-tends equal angles at all points of the circumference, or, otherwise expressed, that the *locus* of the vertices of all triangles on the same side of the same base, with a constant angle at the vertex, is the arc of a circle.

In the primary position, with the visual lines parallel, and the visual plane horizontal, the horopter is formed by the distant vertical view if the retinal meridians are at absolute right angles to each other, or by a horizontal surface below the feet if—as is usually the case—the vertical retinal meridian is not at right angles to the horizontal meridian, but the construction of the horopter in these cases would transgress our limits.[1]

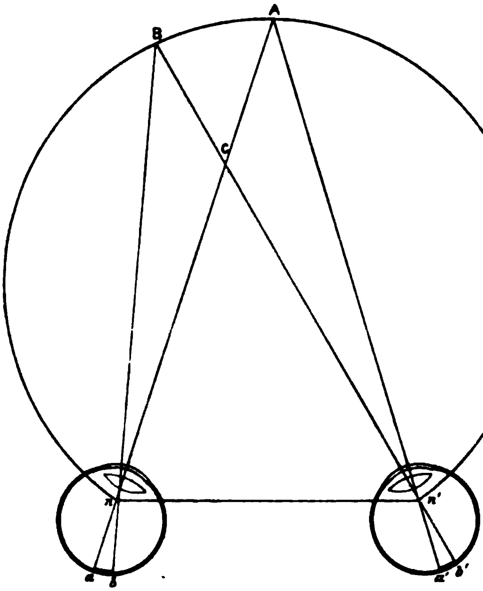


Fig. 221.—To illustrate Müller's Horopteric Circle.

A is the point of regard; its retinal images are formed on the yellow spots at $a\,a'$. $b\,b'$ are corresponding points of the two retinæ, therefore the distance, $a\,b =$ the distance $a'\,b'$. $n\,n'$ are the nodal points of the two eyes. The angles, $a\,n\,b$, $a'\,n'\,b'$, are equal to each other and to the opposite angles, $A\,n\,B$, $A\,n'\,B$; and in the triangles, $B\,C\,n$, $A\,C\,n'$, the opposite angles at C are equal; therefore, in these triangles the remaining angles at A and B are equal. Therefore the point B by which the corresponding images $b\,b'$ are formed must lie in the arc of a circle passing through the points B, n, and n'. Similarly it may be shown that any other point forming corresponding images on the two retinæ will lie in the circular arc $A\,n\,n'$.

---

[1] Students desirous of further information on the subject may refer to Helmholtz, *Physiological Optics*, p. 745; Hering, *Beiträge z. Physiol.* 1864; and in Hermann's *Handbuch d. Physiol.* vol. ~~iv.~~ III

Double vision.—Double vision of an object with both eyes open, is most apparent when the gaze is directed to a point nearer or further than the object, in or nearly in the same line of vision. If a finger is held up in front of the face at arm's length while the eyes are adjusted to a more distant point, the finger will be seen double; closure of the left eye will now abolish the finger apparently seen to the right, and *vice versâ.* If two fingers are held up in front of the face, one at arm's length, the other at half-arm's length, while the eyes are adjusted to distinct vision of the nearer finger, the more distant finger will be seen double; closure of the left eye will now abolish the finger apparently seen to the left, and *vice versâ.*

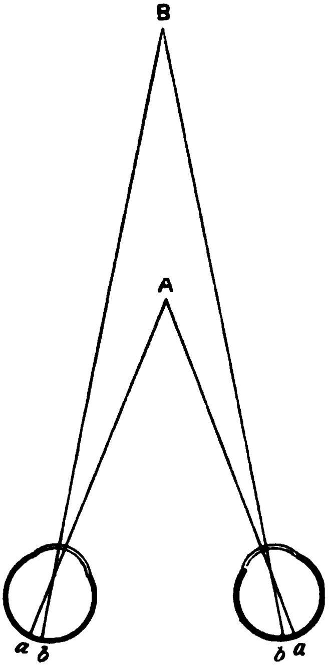


FIG. 222.

Double vision of an object for which the eyes are not accommodated.

The eyes are focussed on B, *i.e.* on the yellow spots at *b b*.

∴ A has retinal images at *a a*.

On closing the left eye, the apparent right finger, A, vanishes.

On closing the right eye, the apparent left finger, A, vanishes.

The eyes are focussed on A, *i.e.* the yellow spots are at *a a*.

∴ B has retinal images at *b b*.

On closing the left eye the apparent left finger, B, vanishes.

On closing the right eye, the apparent right finger, B, vanishes.

Double vision from squint (*Diplopia*).—Double vision also occurs when *both* visual axes are not directed towards an object which is being looked at, *i.e.* when there is squint or *strabismus* of one eye. The subject of squint, when looking at an object, directs to it the visual axis of the sound or working eye, while that of the squinting eye diverges from it, usually to the right or to the left. Consequently the images on the two retinæ are not formed upon corresponding parts; that formed upon the working eye is called the true image, that upon the squinting eye is called the false image. The position of the 'false' in relation to the true image in various cases of misdirection of a visual axis will be best understood when the normal movements have been considered.

Movements of the eyeballs.—As has been stated above, it is a necessary condition to single vision with the two eyes that the objects should form their images upon corresponding parts of each retina—upon the yellow spots when objects are looked at. Now single vision is the normal event and is preserved with all kinds of direction of the lines of vision; its necessary condition is, then, a very delicate co-ordination of the muscles which move the eyes. Each eye is moved by six muscles: four recti—superior, inferior, internal, and external; two obliqui—superior and inferior. The third or motor oculi nerve supplies the superior, inferior, and internal recti, and the inferior oblique; the fourth or trochlearis nerve supplies the superior oblique; the sixth or abducens nerve supplies the external rectus. The eye rotates as a ball in its socket, the centre of rotation being approximately the centre of the eyeball, and the axes of rotation *transverse* to the antero-posterior axis. The eyeball can be rotated in any direction, up, down, out, or in, or in intermediate directions around such transverse axes, but it does not normally rotate to any sensible extent around its antero-posterior axis. These directions are best defined by referring to the direction in which the cornea is moved, and the effects of the individual muscles in

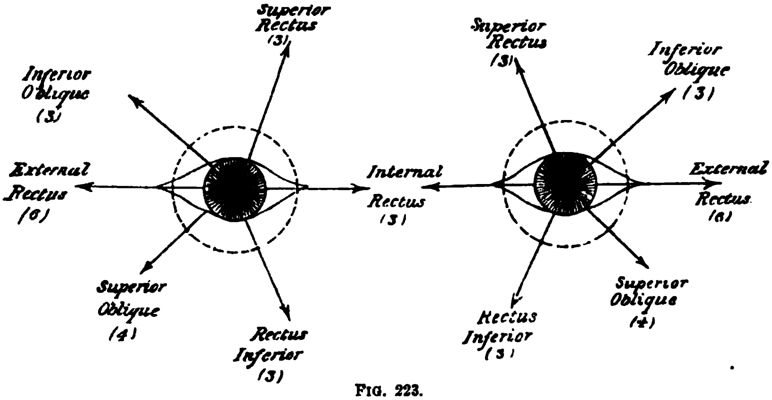


FIG. 223.

Diagram to illustrate the directions towards which the pupil is moved by the separate action of the six muscles of the eyeball. The eyes are turned inwards and outwards by the external and internal recti; the internal rectus of one side is the yoke-fellow of the external rectus of the opposite side in these conjugate movements. The eyes are turned upwards by the superior rectus and inferior oblique, downwards by the inferior rectus and superior oblique.

The eyes are represented facing the observer; if it be imagined that the eyes are looked at from the back, so that the diagram right-left becomes left-right, it will serve to illustrate the displacements in the field of vision caused by paralysis of individual muscles and nerves.

this respect are expressed in the diagram by arrows indicative of the direction towards which the cornea moves.

For the six muscles of either eye it is evident that:—

the internal rectus rotates the eye *inwards*
,, external rectus ,, ,, *outwards*
,, superior rectus ,, ,, *upwards and inwards*
,, inferior rectus ,, ,, *downwards and inwards*
,, superior oblique ,, ,, *downwards and outwards*
,, inferior oblique ,, ,, *upwards and outwards*

and that rotation vertically *upwards* is effected by the joint action of the superior rectus and of the inferior oblique, rotation vertically *downwards* by the joint action of the inferior rectus and of the superior oblique.

The eyeball is thus, as regards its principal movements, a sphere capable of rotating in any direction round its centre, up, down, in and out; vertical movements being effected round a horizontal axis, oblique movements round oblique axes, there being under ordinary circumstances little or no torsion of the globe round its antero-posterior axis. The various axes round which the eye rotates all lie in one plane at right angles to the line of vision and passing through the centre of rotation, the exact position of which is 1·77 mm. behind the centre of the eyeball. This plane is known as Listing's plane.

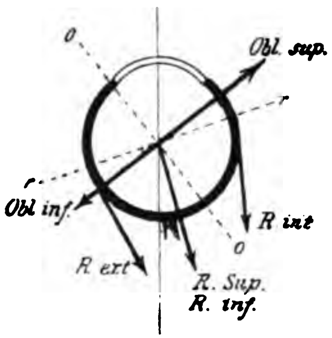


FIG. 224.—HORIZONTAL SECTION OF LEFT EYEBALL.

To illustrate the direction of action and the axes of rotation of its muscles. The arrows indicate the direction of action, the dotted lines indicate axes of rotation. *o o* is the axis round which the eyeball rotates by action of the obliques. *r r* is the axis of the superior and inferior rectus. The axis of the superior and inferior rectus would be represented by a pin through the point of intersection of *o o* and *r r*, perpendicular to the plane of the paper.

Wheel-movements of the iris—true and false.—In these parallel movements there is no rotation of the eyeball round an antero-posterior axis (wheel-movement of iris); the wheel-movement or torsion apparently indicated by the following experiment is not real, but a mixed effect, due in part to an error of judgment, in part to inclinations which a horizontal retinal meridian suffers in oblique movements round oblique transverse axes. It is convenient to refer these effects to 'wheel-movement,' but we must then characterise them as 'false wheel-movements' in distinction from 'true wheel-movements' which do actually take place under certain conditions, viz. with converging visual axes, and with inclinations of the head towards either shoulder while the visual axes are kept fixed; in the first case the two eyeballs rotate *outwards* round the axes of the lines of vision, in the second case the two eyeballs rotate *against* the direction towards which the head is inclined.

The apparent rotation, or false wheel-movement, is demonstrated by means of after-images, as follows:—The observer sits with the gaze fixed in the primary position (*i.e.* head erect—eyes looking horizontally straightforward), opposite to but not too near a grey wall with faint vertical lines; a strip of red paper is fixed vertically against the wall on a level with the eyes. The centre of the strip having been steadily regarded for a few seconds, the eyes are suddenly directed vertically up or down, or horizontally to the right or left. The green-blue after-image of the strip will in all these cases remain vertical; but if the eyes are directed obliquely upwards and to the right, or downwards and to the left, the after-image will appear tilted to the right; if the eyes are directed obliquely upwards and to the left, or downwards and to the right, the after-image will appear tilted to the left.

That these rotations are *apparent* is at once recognised by substituting a horizontal for a vertical red line, 'branding' the retina as before with a green-blue after-image; the latter will be inclined *against* the inclinations of the vertical after-images. Or, if a rectangular cross be taken, the vertical and horizontal components of the after-images will set towards each other. The explanation is as follows:—A rectangular cross seen upwards and to the right, casts a retinal image which is not rectangular but inclined thus , yet it is judged to be rectangular, the actually rectangular brand projected upwards and to the right is therefore misjudged and interpreted as if due to a cross inclined thus ; and similarly for the three other cases —down to right, down to left, up to left. The best way to avoid this complication by misjudgment is to take a single coloured line and a faint lined surface, both movable round a central axis, and to adjust the lines obliquely, in the directions along which the line of vision is to be shifted from the first point of fixation.

From a knowledge of the action of muscles on the eyeball and of the relation between retinal images and apparent position of objects in the field of vision, it is easy to deduce what must be the displacement of the eyeball and the position of false images.

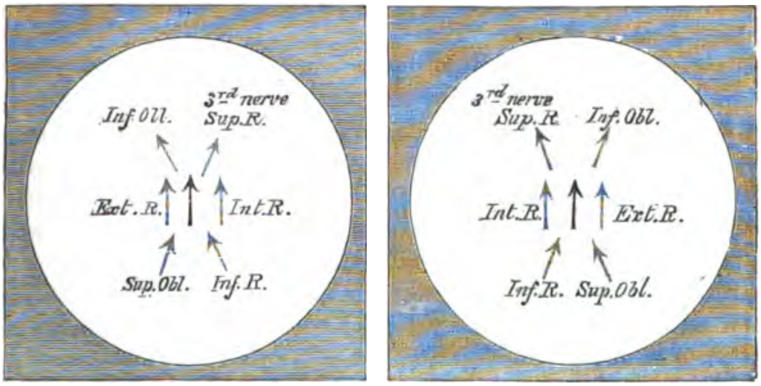
in the field of vision in consequence of paralysis of one or more muscles or nerves.

A simple case is that of the *external rectus*; its action is to rotate the eye outwards, the right eye to the right, the left eye to the left; if it is paralysed the eye will squint inwards, the right eye to the left, the left eye to the right; in consequence of this displacement the image of an object looked at by the patient will fall upon the retina on the internal or nasal side of the fovea, and the apparent image in his field of vision will be on the external or temporal side of the true image; if the right external rectus is paralysed the false image (seen by means of the right eye) will lie on the right side of the true image (seen by the left eye); if the left external rectus is paralysed the false image (by the left eye) will lie on the left side of the true image (by the right eye). In neither case will the false image be tilted, but simply displaced laterally.

Name		Normal action and direction in which movements are defective in paralysis	Direction of paralytic squint caused by excessive action of antagonists	Relation of false image on retina to position it should occupy	Relation of apparent image in field of vision to position of object seen by working eye	Inclination of apparent image to or from working image
Internal rectus . .	3	In	Out	Ext.	In	None
External rectus	6	Out	In	Int.	Out	None
Superior rectus . .	3	Up and in	Down and out	Inf. and ext.	Up and in	From
Inferior oblique .	3	Up and out	Down and in	Inf. and int.	Up and out	From
Inferior rectus . .	3	Down and in	Up and out	Sup. and ext.	Down and in	To
Superior oblique	4	Down and out	Up and in	Sup. and int.	Down and out	To
Third nerve .		Up and in	Down and out	Inf. and ext.	Up and in	From
Internal rectus . .	R	L	R	R	L	None
„ „ . .	L	R	L	L	R	None
External rectus or Sixth Nerve	R	R	L	L	R	None
	L	L	R	R	L	None
Superior rectus . .	R	Up and L	Down and R	Inf. and R	Sup. and L	To L
„ „ . .	L	Up and R	Down and L	Inf. and L	Sup. and R	To R
Inferior oblique .	R	Up and R	Down and L	Inf. and L	Sup. and R	To R
„ „ . .	L	Up and L	Down and R	Inf. and R	Sup. and L	To L
Inferior rectus . .	R	Down and L	Up and R	Sup. and R	Inf. and L	To R
„ „ . .	L	Down and R	Up and L	Sup. and L	Inf. and R	To L
Superior oblique or Fourth Nerve	R	Down and R	Up and L	Sup. and L	Inf. and R	To L
	L	Down and L	Up and R	Sup. and R	Inf. and L	To R
Third nerve .	R	Up and L	Down and R	Inf. and R	Sup. and L	To L
„ „ . .	L	Up and R	Down and L	Inf. and L	Sup. and R	To R

A more complex case is that of the *third nerve*; its action is to rotate the eye upwards and inwards; if the third right nerve is paralysed, the right eyeball squints downwards and to the right; the false image on the retina of that eye will be below and to the right of the yellow spot; the apparent image in the field of vision will be, in relation to the true image, above and to the left. If the third left nerve is paralysed, the left eyeball squints downwards and to the left; the false image on the retina will be below and to the left of the yellow spot; the apparent image in the field of vision will be, in relation to the true image, above and to the right.

Reasoning in a similar manner from the known action of a given muscle, to the displacement which the eyeball will theoretically undergo in consequence, it is easy to construct a table of all the different possible cases, and to embody them in a diagram (fig. 225) constructed from the diagram which represents the movements of the eyeballs (fig. 223). The tilting of the



Left FIG. 225. Right

APPARENT DISPLACEMENTS OF AN OBJECT IN THE FIELD OF VISION IN CONSEQUENCE OF PARALYSIS OF THE SEVERAL MUSCLES OF THE EYEBALL.

The central arrow is the position of the object in the field as viewed by the working eye. N.B.—From the statements in the text it will be evident that fig. 225 may be constructed from fig. 223. The latter viewed by transparency or in a mirror gives the construction of the former. It will thus be realised that (1) the displacement in consequence of the paralysis of any muscle is the converse of its displacement by the action of that muscle; (2) the accompanying displacement of the false image in relation to the true image, in consequence of paralysis of a muscle, is in the same direction as the normal action of that muscle.

These rules apply equally to the resultant effects of any nerve and of any group of muscles. Practically, however, the immense majority of cases which actually present themselves are those which are indicated by heavy type in the table, and in connection with these common cases the effects are usually complicated by collateral effects, the description of which belongs to ophthalmology. One of these collateral effects is of physiological import, and may therefore be alluded to here. In normal conjugate movements of the two eyes, *e.g.* to the right or left, the external rectus of one eye acts with the internal rectus of the opposite eye (*v.* p. 516); if, for instance, the right external rectus is paralysed, the right eye squints inwards, and cannot be directed to the left, but the attempt to do so causes an excessive action of its yoke-fellow, the left internal rectus, and the left or normal eye now squints inwards. This is called a secondary squint, and has been compared to the effect which would be produced in driving a pair of horses with unequally sensitive mouths—an effort to turn the pair would cause the normal horse (or normal eye) to deviate much more than the hard-mouthed horse (or paralysed eye).

image (which is *not* the result of any torsion of the eyeball on its antero-posterior axis) is also indicated by the same diagram.

Movements of the iris.—Allusion has already been made to the fact that the iris plays the part of a circular muscular diaphragm controlled by nerves. Experimentally it is found that the central aperture or pupil is diminished by excitation of the third nerve, and by section of the cervical sympathetic—increased by excitation of the sympathetic, and by section of the third nerve; it is usually assumed that the iris is composed of circular or constrictor fibres, and of radiating or dilatator fibres, the third nerve being the motor nerve of the circular muscle, the sympathetic the motor nerve of the radiating fibres. But it must be admitted that the anatomical existence of radiating fibres is not well established—in fact, the chief evidence of their existence is to be found in the physiological effects of section, and of excitation of the cervical sympathetic—and there is therefore room for an alternative hypothesis to the effect that the iris possesses only a circular or sphincter system of fibres, to which the third nerve is motor and the sympathetic inhibitory. The actual evidence in favour of this hypothesis is as follows: Direct electrical excitation of an excised iris may cause shortening or elongation, *i.e.* increased contraction or diminished contraction (Grünhagen).

Movements of the iris also take place in association with accommodation, in response to various stimuli, and in consequence of the administration of certain drugs. Stimulation of the retina by light, or experimental excitation of the optic nerve, causes reflex contraction of the pupil, and on the higher mammalia (dog, cat, and man), with incomplete decussation of the optic nerves, both pupils contract when the retina or optic nerve of one side is stimulated. In cases of locomotor ataxy reflex contraction of the iris may fail to occur, although the pupil contracts during the act of accommodation (paradoxical reaction or Argyll-Robertson pupil).

Stimulation of the skin, painful impressions, many forms of emotion—such as surprise or awakened attention—muscular exertion, dyspnœa, give rise to dilatation of the pupil; during sleep on the contrary the pupil is contracted. After section of the sympathetic, cutaneous stimuli no longer cause reflex dilatation, and the pupil dilates much more slowly on removal of light. If the third nerve and the sympathetic be simultaneously and equally excited, the action of the latter predominates, and the pupil dilates. When death takes place the pupil is for a short time dilated, and subsequently contracted; if the cervical sympathetic is divided on one side before death,

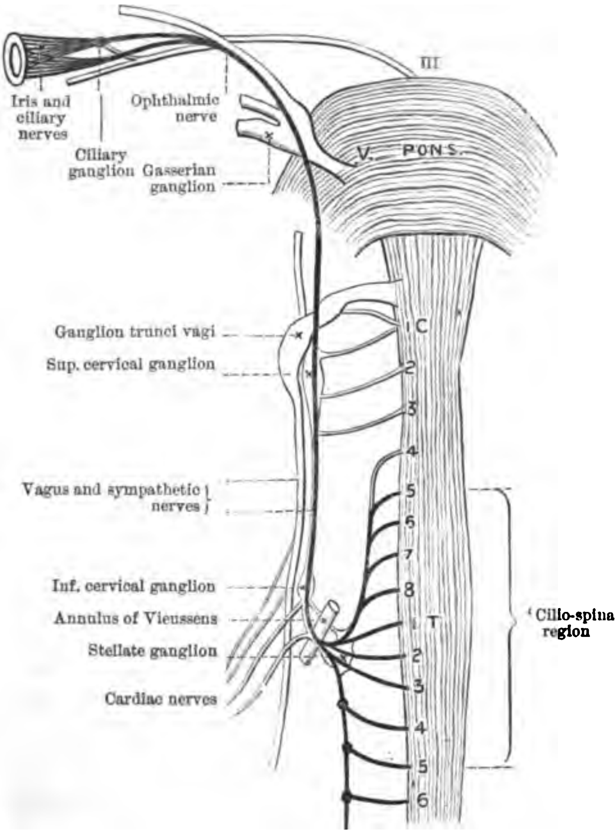


FIG. 226.—DIAGRAM TO ILLUSTRATE THE PATHS OF INNERVATION OF THE IRIS.

Constrictors from the corpora quadrigemina by the 3rd nerve, ciliary ganglion and nerves to the circular muscle of the iris. Dilatators from bulb and cord by anterior roots, rami communicantes, cervical sympathetic and ganglia, Gasserian ganglion ophthalmic branch of the 5th nerve, ciliary ganglion, and nerves to radiating (?) muscle of iris.

dilatation of the pupil on that side does not occur post mortem. Among drugs the chief constrictors are morphia and eserin, the chief dilatators atropin and cocain. Excitation of the third nerve of an atropinised eye produces no effect. Nicotine causes a brief dilatation followed by a prolonged constriction; excitation of the cervical sympathetic now produces no effect, whereas excitation above the superior cervical ganglion dilates the pupil as usual (Langley and Dickinson). Langendorff has shown that at death excitation below the ganglion ceases to be effectual before excitation above the ganglion. Waller showed in 1853 that the divided cervical sympathetic degenerates up to the superior cervical ganglion, and that four or five days after section its excitation produces no effect on the pupil, while excitation of the ganglion itself produces the usual dilatation. Movements of the pupil in consequence of variations of light, or of drugs locally applied, will continue to occur in the excised eyes of cold-blooded animals. If a frog's eye be kept for a few minutes alternately in the dark and in the light, the pupil will become obviously larger and smaller.

The muscular fibre of the iris is of the non-striated kind (except in birds). Its nerves reach it by way of the ciliary branches of the ophthalmic division of the fifth, which contain fibres derived from that nerve (sensory), from the third nerve (constrictor), and from the sympathetic (dilatator). These last have been experimentally traced back through the Gasserian ganglion to the cervical sympathetic, and through the last cervical and first thoracic ganglia to the spinal cord through the anterior nerve-roots from the fifth cervical to the fifth thoracic. The region of the cord from which they spring has been termed the *cilio-spinal region* (Budge and Waller), and is subordinate to a bulbar centre above. A few fibres springing from the bulb pass directly to the eye by the channel of the fifth nerve. According to Gaskell the dilating nerves of the iris are composed of fine medullated fibres similar to the dilating nerve-fibres of the blood-vessels, and lose their medullary sheath in the superior cervical ganglion.

Retinal shadows.—Foreign bodies in the eyeball may, under certain conditions, cast shadows on the retina, and it is possible in various ways to cause the retinal vessels themselves to throw their shadows upon the retina. Such shadows, however produced, excite in consciousness the impression of objects in front of the eye. To determine the presence of foreign bodies, focal illumination of the eye should be employed, *i.e.* the light should be placed at that point in front of the eye to which parallel rays emerging from the eye would come to a focus; the eye is thus illuminated by a cylinder of parallel rays from pupil to retina, and a foreign body then causes a retinal shadow, which appears as a dark mass in a bright circular field. By ascertaining the direction and extent to which a given shadow alters its position in the bright field when the light is moved up or down, it is possible to form a very accurate judgment of the position of the foreign body in the eye. If the foreign body is in the same plane as the iris, its shadow will preserve its relative position in the bright disc. If it is on a plane *anterior* to that of the iris, the shadow will appear to rise and fall as the light is raised or lowered. If it is on a plane *posterior* to that of the iris, the shadow will appear to rise and fall as the light is lowered and raised. In this last case the object appears to move in an opposite sense, while in the second case it appears to move in the same sense, with reference to the direction in which the light is moved (see fig. 227). In any case the extent of apparent movement is in proportion to the distance of the foreign body from the plane of the pupil; if, for instance, it is very near the retina, a small movement of light may bring the shadow up to or beyond the edge of the bright disc.

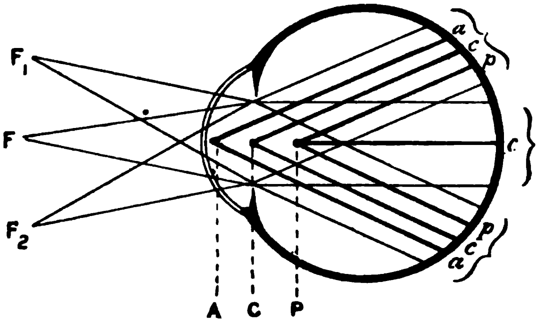


FIG. 227.—POSITION OF FOREIGN BODY ASCERTAINED BY MOVEMENT OF THE SHADOW FORMED WITH FOCAL ILLUMINATION.

	Light raised to F_1	*Light lowered to* F_2
The foreign body is in front of the plane of the iris at A.	Shadow moved towards lower border of retinal disc, *i.e. upwards* in the bright field.	Shadow moved towards upper border of bright disc, *i.e. downwards* in the field.
The foreign body is behind the plane of the iris at P.	Shadow moved towards upper border of bright disc, *i.e. downwards* in the field.	Shadow moved towards lower border of bright disc, *i.e. upwards* in the field.

Slight shadows caused by small specks or imperfections of the media are common to most eyes, they move with the movements of the eye when attempts are made to look at them; hence their name—*muscæ volitantes*.

Shadows of the retinal vessels may be made apparent in various ways (Purkinje):—(1) A strong light is focussed upon the sclerotic just outside the cornea, the eye being wide open, directed towards a dark background; in a few seconds, especially if the light is kept slightly moving, the arborescent pattern of the retinal vessels will be plainly seen. The mode in which a retinal vessel casts its shadow on the retina, and the direction in which the shadow moves and the vessel appears to move, are illustrated in fig. 228.

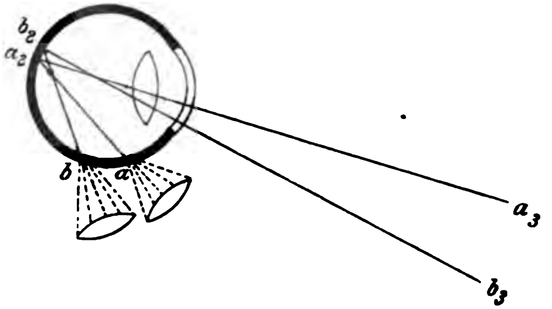
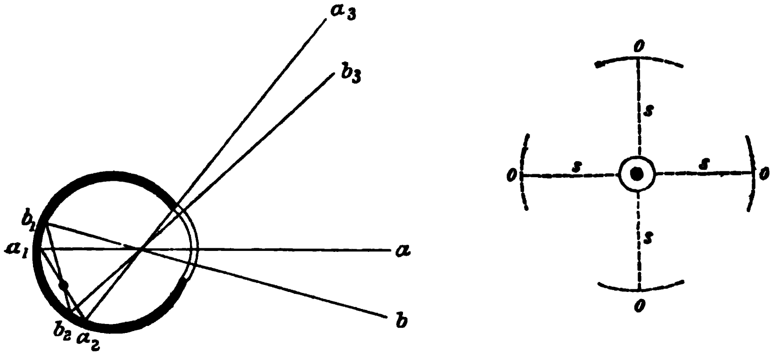


FIG. 228.—PURKINJE'S NETWORK MADE VISIBLE BY ILLUMINATION THROUGH THE SCLEROTIC.

The spot of light, a, gives the shadow, a_2, of the vessel which is apparent at a_3; if the spot of light is shifted to b the shadow of the vessel is at b_2, and is apparent at b_3, *i.e.* the vessels appear to move in the same direction as the spot of light (Helmholtz).

(2) A readier though less perfect method of taking cognisance of one's own retinal vessels, is to fix the gaze upon a dark background in a darkened room, while a candle is moved slightly up and down or from side to side close to the cheek. The arborescent shadow of the retinal vessels will soon be apparent—most plainly so the horizontal vessels if the candle is moved up and down, the vertical vessels if the candle is moved from side to side. It will be noticeable, moreover, that with vertical movements of the candle held laterally on a level with the eye, the apparent movements of the vessels will be opposite in direction to those of the candle, *i.e.* the vessels appearing to sink in the field as the candle is raised, to rise in the field as the candle is lowered; with lateral movements of the candle the apparent movements of the vessels will be in the same sense as those of the candle.

The mode in which shadows are formed by this method differs from the preceding one in that the illumination is through the cornea, the light being imperfectly focussed at a_1, where it forms an illuminating spot analogous to the illuminating spot a in the previous diagram.



FIGS. 229 and 230.—PURKINJE'S NETWORK MADE VISIBLE BY ILLUMINATION THROUGH THE CORNEA.

Light from a is imperfectly focussed at a_1, where it forms an illuminating spot. A shadow, a_2, is formed of the vessel and is referred to a_3 in the field of vision. Considering the diagram to represent a horizontal section of the eye, if the light is moved laterally to b, the illuminating spot in the eye becomes b_1, the shadow of the vessel is at b_2, and the vessel appears to move to b_3 in the field of vision, *i.e.* in the same direction with lateral movement of the light; if, on the other hand, the light be shifted vertically, *e.g.* upwards from a (above the plane of the paper), the illuminating spot a_1 will be lower, the shadow a_2 higher, the apparent vessel a_3 lower, than the plane of the paper, *i.e.* the vessel appears to move against vertical movements of the light (Helmholtz).

More generally stated, so as to include all kinds of positions of light and directions of apparent movement, the relation is as follows: the apparent movement is homonymous when the light is moved in any plane containing the line of vision, and reversed when the light is moved in an arc round the line of vision. If in fig. 230 the circle represents the cornea, its centre the transverse section of the visual line (perpendicular to the paper), a movement of the light along any radius, *s s*, will give similar apparent movement; a movement along any portion of the circle, *o o*, will give opposite apparent movement.

Phosphenes, or false lights.—The retina and optic nerve can be excited by mechanical or electrical stimuli; the sensations to which these give rise are known as *phosphenes*, and are presented subjectively as flashes of light. If the butt end of a pencil is pressed against the nasal side of the retina while the eye is directed upon obscurity, a circular bright phosphene appears on the temporal side of the field of vision; similarly pressure on the temporal, upper or lower sides of the eyeball causes sensations of light referred to the nasal, lower or upper parts of the field of vision. The sudden relaxation of accommodation may be sufficient to excite the retina mechanically; the phosphene so produced has the form of a circle. Electrical excitation of the eyeball or of the optic nerve likewise gives rise to phosphenes occupying the whole field of vision, effects which follow the application of either pole of interrupted or of constant currents. Any exact study of polar effects is however impracticable, owing to the unavoidable complexity of current distribution when the electrode is applied to the eye. The flash is, if anything, most pronounced at make when the kathode is on the eyeball, at break when the anode is substituted for it (the second or indifferent electrode being in the mouth). If a fine pointed kathode is applied to the temporal side of the eyeball, the nasal half of the field of vision of that eye appears bright in comparison with the temporal half; *vice versâ*, if an anode be so applied, the temporal half appears brighter than the nasal half.

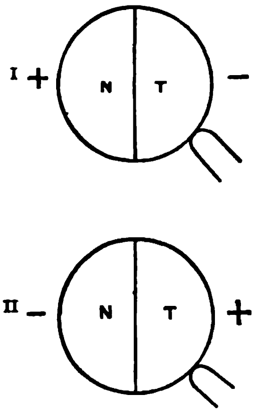


FIG. 231.

I. Excitation increased in temporal side of retina. Excitation diminished in nasal side of retina. Nasal side of field bright. Temporal side of field obscure.
II. All reversed.

Objective effects of light upon the retina.—We have hitherto considered the subjective effects of light acting upon the retina; there remain to be described certain objective effects of the same cause, which can be appreciated by physical examination. These are: (1) Bleaching of the 'visual' purple. (2) Movements of pigment cells. (3) Movements of cones. (4) Electrical changes.

The effect of light upon the pigment cells of the retina is exactly the opposite to its effect on the pigment cells of the skin. In a retina which has been protected from light before and during removal, the pigment is concentrated in the body of the cells, whereas after exposure to light the pigment is scattered to a considerable distance between the rods—unlike the pigment in the frog's skin, which is concentrated in the cell under the influence of light, diffused when the skin has been protected from light. The retinal pigment above alluded to has received the names of *melanin* or *fuscin*; it is the source from which the retinal purple is derived.

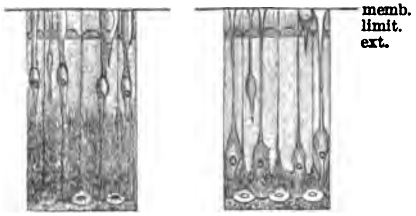
In addition to *fuscin*, several other pigments have been identified in the retina, viz. *rhodopsin*, which is confined to the outer part of the rods, and *chromophanes* (red, green and yellow), which are coloured oil globules situated in the inner segments of the cones. All these pigments are sensitive to light, being bleached by it, but they are not always present in all animals; rhodopsin is not present in the retinæ of many birds, chromophanes are not present in mammalia, nor is there any relation between the presence of these pigments and the nocturnal or diurnal habits of animals.

The pigment of most interest, and which has been most studied, is rhodopsin or the retinal purple, which can be readily seen colouring the inner surface of the retina of a frog or of a rabbit kept in obscurity for some time previously; the removal of the eye and of the retina should be carried out in darkness, or, at most, by the aid of a sodium flame. If we expose one eye to ordinary daylight while the other is kept in darkness, the retina of the first eye will be found of a much paler hue, 'bleached,' in comparison with that of the protected eye, the change being much more rapidly brought about in the case of the rabbit's than in that of the frog's eye (Boll. Kühne). If this bleached eye be replaced in darkness, and again examined a short time after, it will be found that the retina has partially or wholly recovered its original pink colour. If, however, this last experiment be repeated with a retina, which has been removed from the eye and separated from its layer of pigmented epithelium, the recovery of colour will not take place. From this, we learn that the presence of the brown pigment (fuscin) in the outermost layer of the retina is the stock from which is derived the purple pigment (rhodopsin) in the rods.

The retina can be bleached locally in patterns by causing appropriate images of light to be focussed on its surface. By means of a 4 per cent. solution of potash alum, retinal pictures thus produced—*optograms*—can be fixed so as to remain unaltered by the further action of light. The visual purple has been extracted from the retina by means of a 2½ per cent. solution of bile-salts, as a coloured solution which is sensitive to the action of light (Kühne).

That the retinal purple bears no demonstrable relation to vision is shown by the facts that (1) animals devoid of purple, or moving about in a light so strong that it must have bleached every trace of purple, can see; and (2) retinal purple is absent from the yellow spot, which contains cones only. The popular name 'visual' purple is therefore a misnomer.

Van Stort and Engelmann state that the outer limbs of the cones vary according as preparations are taken from retinæ which have been exposed to or protected from light. If the retina has been protected from light, the cones protrude right down to the pigmented layer; if it has been exposed to light, they are retracted and sessile upon the external limiting membrane. Engelmann states further that this retraction of the cones is directly controlled by nerves—illumination of one eye or of the skin producing reflex retraction of the cones of a protected eye, strychnia poisoning and general faradisation causing the cones of both eyes to be retracted in the absence of light. The electrical effects of retinal excitation have been described at p. 392.



After 5 min. exposure to daylight pigment diffused, cones retracted.

In darkness; pigment concentrated, cones protruded.

FIG. 232.—ACTION OF LIGHT UPON RETINA. (Engelmann.)

The Ophthalmoscope.—The ophthalmoscope is used to examine the fundus of the eye, more particularly the optic disc and the retinal vessels, and to detect and estimate errors of refraction. For the examination of the retina the 'indirect' or the 'direct' method may be adopted: the former is the more generally serviceable, and yields a reversed image of a considerable area of the retina magnified about five times; the latter is useful for more minute examination, and yields an erect image of a small area of the retina magnified about twenty times. To estimate refraction the direct method must be adopted.

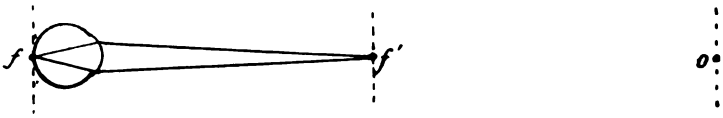


FIG. 233.

An eye accommodated for a given point *f'* is equivalent to a lens with conjugate foci at the point *f'* and at the fovea—*f*. An object in the plane *f'* has its real reversed image focussed small in the plane *f*; conversely an object in the plane *f* (*e.g.* a retinal vessel) has its real reversed image focussed large in the plane *f'*. The conjugate focus *f'* can by strong accommodation of the observed eye be made to coincide with the 'near' point of that eye, and may be seen by an observing eye at o. The smallest distance at which an image in the plane f' can be seen clearly by an observer is the near point of the observer's eye. Thus the minimum distance at which focussing is possible with accommodation of the observed and observing eyes is about ten inches.

If the converging power of the observed eye be increased by a convex lens (15 to 20 D) placed in front of it (accommodation being now unnecessary), the conjugate foci of the system will be as under, f' being brought close to the eye, and a retinal vessel in the plane f will have its real reversed image nearer to the eye in the plane f'. An observing eye placed at o (so that the distance o f' is greater than that of the observer's near point) could see this image of the retinal vessels if the retina were a source of light or lighted up so as to reflect sufficient light. This can be done. The fundus of the eye is made visible by rays reflected from the mirror which light up its vessels, &c.; rays reflected from parts so illuminated emerge from the observed eye and form the image f', which is seen by the observing eye.

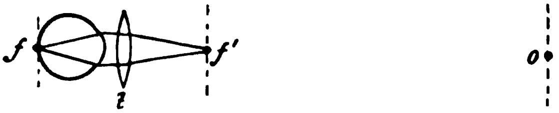


FIG. 234.

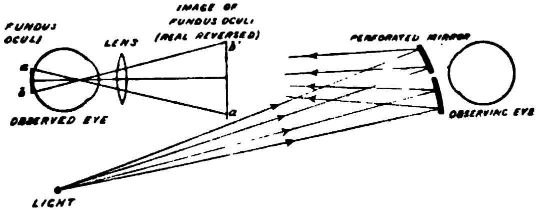


FIG. 235.—DIAGRAM TO SHOW HOW OBJECTS ON THE FUNDUS OCULI ARE ILLUMINATED AND SEEN BY THE INDIRECT METHOD.

The lines of vision and of illumination are made to coincide by the perforated mirror, which is concave in order to concentrate the light.

The main principle upon which the ophthalmoscope depends is thus that the line of vision of the observing eye shall be in the line of illumination. This is effected by means of a perforated mirror through which the observer looks while he directs light in the direction of his line of vision.

This method of examination is known as the *indirect method*. The retinal object, *a b*, is illuminated by light reflected from a concave perforated mirror; rays reflected from the bright object, *a b*, are refracted by the observed eye and auxiliary lens to form a real reversed image, *b′ a′*, which is looked at by the observing eye through a hole in the mirror (fig. 235).

The second method of examination is known as the *direct method*; the image thus obtained is a virtual erect image formed by rays as they emerge from the observed eye. In this case, to obtain any useful view the observing and observed eye must be as close as possible. As will be understood from the description of the three conditions of refraction which we may have to deal with, the 'direct method' is one of the means of detecting and estimating errors of refraction.

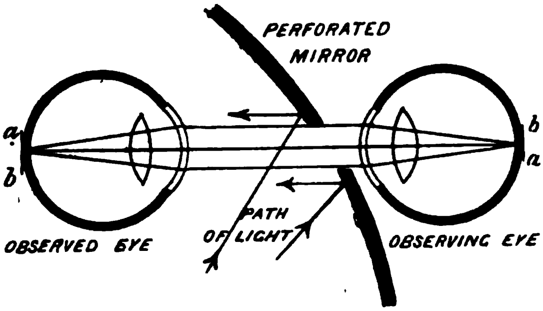


FIG. 236.—DIAGRAM TO SHOW HOW OBJECTS ON THE FUNDUS OCULI ARE ILLUMINATED AND SEEN BY THE DIRECT METHOD.

Both the eyes are supposed to be emmetropic and non-accommodated.
The size of the mirror aperture is greatly exaggerated.

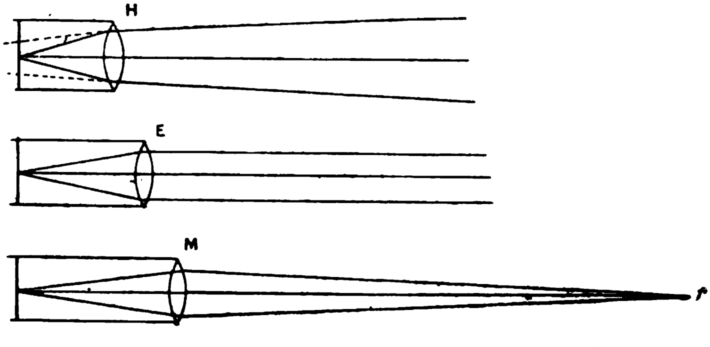


FIG. 237.—PATH OF RAY EMERGING FROM A HYPERMETROPIC, FROM AN EMMETROPIC, AND FROM A MYOPIC EYE.

From the emmetropic eye, E, with relaxed accommodation, the rays will be parallel and give no image.

From the hypermetropic eye, H, the rays will be divergent, and, being prolonged backwards, give a virtual erect image.

From the myopic eye, M (or from an accommodated emmetropic eye), the rays will be convergent and give a real reversed image at *f*.

Rays emerging from any given point at the fundus of a normal eye will be parallel, from a short eye they will be divergent, from a long eye they will be convergent. Such rays will not come to a focus in the case of the normal eye (so long as its accommodation is entirely relaxed), they will have a virtual focus in the case of the short eye, a real focus in the case of the long eye; in the first case (E) no image of the retinal surface is formed, in the second (H) a virtual erect image is formed behind the eye, in the third (M) a real reversed image is formed in front of the eye (fig. 237).

The chief practical difficulty in the use of the direct method is for the observer to maintain his eye non-accommodated. Thus to estimate hypermetropia he has to find the strength of the convex lens which, added to his non-accommodated eye, gives distinct vision of the fundus, and it is therefore essential that he should not unconsciously exert any effort of accommodation. For the minute examination of a normal eye by the direct method the observer's eye must be non-accommodated, for a myopic eye it must be less than non-accommodated, *i.e.* the assistance of a concave lens is required; on the other hand, for a hypermetropic eye the observer has to accommodate or to use a convex lens behind the mirror.

The observed eye must also be non-accommodated in order that its refraction may be estimated, and also for the minute examination of the fundus. Whereas rays emerging from a normal non-accommodated eye are parallel, rays emerging from a normal accommodated eye will be converging, *i.e.* such an eye will be equivalent to the myopic eye, and its vessels will not be seen by close examination unless a concave lens is used behind the mirror. Hence it will be understood that in the direct examination of the fundus: (1) a concave lens must be added behind the mirror if the observed eye is myopic; (2) a weak concave lens may be added if the observed eye is normal, in which case the observer accommodates the fundus; (3) a convex lens may be used if the observed eye is extremely hypermetropic.

Relations of light perception to retinal stimulation.—The subjects now to be considered occupy a borderland position between the physiology of the retina and that of the brain. In every subjective study of sensation and in most objective experiments we study in one combined group, sense-organ, sensory nerve, and sensory centre. The analysis of any sensation must therefore trench upon cerebral physiology, and that of visual sensation does so in highest degree; developmentally and anatomically, as well as physiologically, the retina is the most closely cerebral of our sense-organs; and judgments from visual data form a larger contribution to our daily experience than the judgments derived from all other sensory data put together. We shall in a further chapter make use of these data in general illustration of the formation of judgments, and shall then give an account of the leading theories into which the facts have been interpreted; at present we shall simply state these facts as they have been observed, without asserting that they are cerebral or retinal or photochemical or psychical. In this allusion to theories, we refer particularly to the phenomena of simultaneous contrast, which are described below, and further discussed at p. 545.

The shortest known flash of light, that of the electric spark (of which the duration is less than one millionth of a second), is long enough to produce a sensation, the duration of the latter being very much greater. The sensory effect outlasts its physical cause. Definite numbers expressive of the *duration* of the sensory effect cannot, however, be exactly assigned, as it varies greatly with the strength of stimulation and with the state of the retina.[1] Very strong stimuli give rise to effects so prolonged as to be characterised as after-effects (positive). Many illustrations of this relation between stimulus and sensation are matters of every-day experience. (1) A luminous body, *e.g.* a firebrand, rapidly whirled round, causes the sensation of a fiery circle; different retinal points are excited in such rapid succession that the first made sensations are still in force when the last made sensations appear. (2) A disc of two colours, if rapidly rotated, is seen of a uniform resultant colour, *e.g.* if the two colours are complementary the resultant is in the direction of white; the same retinal points are alternately excited by the two colours in such rapid succession that the sensations of both co-exist and are fused in consciousness. (3) A succession of stimuli such as that produced by the rotation of a black disc with white sectors produces a sensation analogous with muscular tetanus, *i.e.* infrequent stimuli are perceived separately, more frequent stimuli are perceived incompletely fused, and, finally, stimuli above a given limit of frequency give rise to a perfectly uniform sensation; this last is analogous with complete tetanus, the incompletely fused 'flickering' sensation with incomplete tetanus or muscular clonus, the separate sensations with separate muscular contractions. If the white sectors are strongly lighted, the *minimum frequency* may reach fifty stimuli per second before complete uniformity of sensation is reached; with a weak light, the minimum limit may be as low as ten per second.

---

[1] It would be more correct to say 'of the retino-cerebral apparatus;' but the abbreviation is sanctioned by long use.

Strength of stimulus and strength of sensation are not directly proportional. With strong stimulation a larger increment is requisite to excite the sensation of difference than with weak stimulation; or, to use a concrete instance, the difference of one candle between two lights of 9 and 10 candle-power respectively will be very obvious, while there will be no perceptible difference between two lights of 1,000 and 1,001 candle-power. Otherwise expressed, the amount of stimulus requisite to excite a perception of difference between two stimuli, bears a constant relation to their magnitude, which can be expressed in the form of a fraction. The value of this fraction in the case of light is $\frac{1}{100}$, *i.e.* we can see a difference between two lights of 10 and 10·1, or of 100 and 101, or 1,000 and 1,010 candle-power. A difference of one candle is an obviously large difference when the lights are of the first-named magnitude, it is a just perceptible difference when they are of the second-named magnitude, it is quite imperceptible between lights of the third-named magnitude.

After-images.—We have alluded to positive after-images as being simply an instance of after-sensation; they are called 'positive' because their lighting is similar to that of the original visual images, and in contradistinction from a second variety of after-images in which the shades of the original picture are reversed; images of this kind are negative after-images, which depend for their production upon retino-cerebral fatigue. They may easily be elicited. If, for instance, a well-lighted white pattern on a black ground be steadily gazed at for 10 to 15 seconds, a negative after-image consisting of a dark pattern on a light ground will appear when the gaze is transferred to any uniform surface. Negative after-images are likewise produced by coloured patterns, and in this case the colour of the after-image is complementary to that of the original object: *e.g.* the after-image of a red pattern is green; of green, red; of blue, orange; of orange, blue, &c.

The following after-image experiment shows that an apparently completely saturated colour may be subjectively more fully saturated. A small green disc is gazed at for a few seconds, the eyes are then turned towards a saturated red ground; the red after-image of the green disc is redder than the surrounding red field. On the Young-Helmholtz theory this is attributed to fatigue of the cones excitable by green, and the consequent greater purity of the red excitation in the retinal area which has been covered by the green image. Similar results have been obtained with pure spectral colours, and lead to the conclusion that the most saturated objective colours do not with the non-fatigued eye produce the maximum sensation of saturated colour.

Negative after-images are the most obvious sign of retinal—or properly speaking—of retino-cerebral fatigue; another sign of this process can be appreciated during the contemplation of objects. An object which is just visible in a dim light may be lost sight of if an attempt is made to fix the eyes upon it; at nightfall the horizon between sea and sky may fade out of sight when a prolonged attempt is made to define it, although the line of separation may remain quite perceptible by indirect vision. A star of just perceptible magnitude may become invisible as an attempt is made to keep it in view, though it reappears as soon as the line of vision is diverted by a few degrees. This last observation, well known to astronomers, is probably to be explained as due to the dull excitability of the fovea centralis of the retina. All the observations above cited show that a stimulus of constant intensity produces, if prolonged, a diminishing excitation.

Contrast.—A sheet of 'white' note-paper appears very white against a black background, but far short of white against fresh fallen snow. A piece of red cloth appears redder on green turf, less red against a red background. A yellow skin looks white by the yellow light of gas. These are instances of contrast and of absence of contrast between simultaneous impressions, in consequence of which white, red, and yellow appear to be more or less white, red, and yellow according to circumstances.

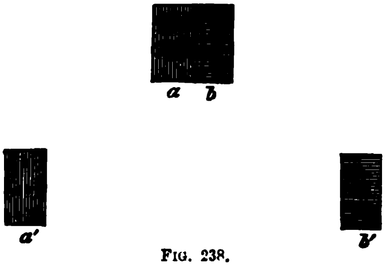


FIG. 238.

A simple but rough way of studying contrast is that which was first adopted by Chevreul. Two slips, *a* and *b*, of coloured paper are fixed side by side; two similar strips, *a′* and *b′*, are fixed at a distance from the first pair. Comparing *a* with *a′*, we see an apparent difference, which is due to the influence on the sensation from *a* of the sensation from the adjacent slip *b*. Similarly by comparing *b* with *b′*, we are made sensible of the influence of *a* upon *b*. Each colour, *a* or *b*, will appear as if mixed with a certain proportion of the complement of the other colour, *b* or *a*, *i.e.* their difference is increased.

The experiment of coloured shadows further illustrates this principle. A rod is fixed so as to throw upon a white screen the shadows (1) of daylight admitted through a hole in a shutter, (2) of candlelight. The first light is white and illuminates the screen with the exception of the portion occupied by the first shadow; the second light is yellow and illuminates the screen with the exception of the second shadow; so that light 1 (white) illuminates shadow 2, light 2 (yellow) illuminates shadow 1. Objectively then shadow 2 should be grey, shadow 1 should be yellow, and the rest of the screen should be pale yellow.

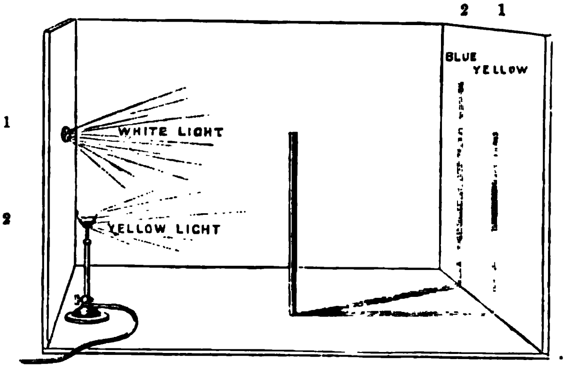


FIG. 239.

As seen, however, shadow 2 is not grey, but *blue*, in contrast with the yellow screen and still more yellow shadow 1.

Or again: Four candles placed in a row illuminate a white screen in a dark room. A second screen is partly interposed between the candles and the first screen, on which we therefore have four vertical strips illuminated by 1, 2, 3, and 4 candles respectively. Each strip is uniformly illuminated throughout, yet it does not appear so. The border of a strip nearest to a darker neighbour looks lighter than the border nearest to a lighter neighbour.

Contrast colours are far more effectively excited by pale than by saturated colours. This is easily verified by the following experiment (H. Meyer). A patch of grey paper placed on a sheet of green paper appears little or not at all altered in tint, but if both papers are covered with thin white tissue paper, whereby the green colour is much weakened, the grey patch at once assumes the contrast tint, pale red. This result, which is at first sight very surprising, illustrates the fact that differences of sensation are much greater with weak than with strong stimulation, so that any error in the sensory estimate is exaggerated when the sensation and the contrasted counter-sensation are weak. Saturated colours in a painting modify greys and whites less than do pale colours.

All the examples given above are examples of *simultaneous* contrast, in which the exciting cause on one portion of the retina modifies cerebral sensations derived from a different portion of the retina, the compared lights or colours being viewed simultaneously. But under ordinary circumstances the eye wanders, so that the effect of simultaneous contrast is reinforced by negative after-effects, which constitute the phenomenon of *successive* contrast. In this case colours fall in succession upon the same portion of the retina, each colour modifies the subsequent colour in this sense that the second colour appears as if mixed with a certain proportion of the complement of the first. The consequence of the first excitation is a negative after-effect or after-image, which becomes fused with the second excitation. As already stated, the after-effect of green is its complement red, so that if after looking at a green surface we look at any other colour, that colour appears to contain less green or more red. The effect in successive contrast is thus simply what we are already familiar with under the name of negative after-image.

We are very liable to get effects in which successive and simultaneous contrasts both take part; it is extremely difficult to keep the eye steady for many seconds at a time; the eye wanders, and we then obtain the contrasting excitations successively in the same part, instead of simultaneously on different parts of the retina. Finally the observation should be made that a negative after-image, as a successive contrast effect, may give rise to a surrounding effect negative to itself as a simultaneous contrast effect. Thus a green pattern gives a red after-image on a greenish background; the red after-image being the complement of the green pattern (successive contrast), the greenish background being the complement of the red after-image (simultaneous contrast). The theoretical significance of these phenomena will be discussed in connection with sensory comparisons and inferences.

Binocular effects.—It is possible to obtain a contrast-effect upon one eye by the chromatic stimulation of the other eye. A slip of white paper on a black background and seen double, with a blue glass in front of the right eye and a grey glass in front of the left eye, appears blue to the former and yellow to the latter. It is also possible, with the adoption of suitable precautions, to obtain the mixture of two colours separately presented to each eye. To this end it is necessary that the coloured surfaces should be perfectly even and unlimited by any outlines. The mixture is less perfect than that which is obtained by causing the two colours to coincide upon the same retina, and at the first attempts to observe it we are liable to alternate attention to one or the other eye and see almost exclusively one colour or the other, or a patchwork which appears as a polished surface; but even at its best the binocular mixture is less complete than the monocular effect, and always darker. (Hering.)

CHAPTER XIII

SOUND AND HEARING

PAGE
452 **Physical data.**
Noise—Musical sound—Strength—Pitch—Timbre—Speed—Wave-length—Resonation—Consonance of strings or membranes—Overtones or upper partial tones—Beats—Undertones or beat tones—Concord and discord.
455 **The ear.**
External, middle, and internal ear—Membrana tympani—Ossicles—Tensor tympani—Stapedius—Eustachian tube—Hearing *viâ* the cranium.
The internal ear—Semicircular canals—Cochlea—Membrana basilaris—Organ of Corti—Hair cells—Theories.

OTHER SENSES

463 **Taste—Smell—Touch—Cutaneous sensation—'The muscular sense.'**
The semicircular canals—Equilibration.

Physical data.—*Sound* is a sensation produced in the organ of hearing by vibrating bodies. Vibrations may be seen, felt, and *heard*; when they are heard, we call their resultant a *sound*. Irregular vibrations cause noises, regular vibrations cause musical sounds.

Musical sounds or tones differ in *intensity* or *strength*, in *pitch*, and in *timbre* or *character*. Intensity depends upon amplitude of vibration, pitch depends upon the number of vibrations per unit of time, timbre depends upon the upper partial tones which accompany a fundamental tone.

Sounds of all strengths travel at the rate of 1,100 feet (330 meters) per second in air of 15° Centigrade. Given the speed at which sound travels and the number of vibrations per second, it is easy to calculate the *wave-length* of a single vibration. Thus the wave-length in a note of 11 vibrations per second will be 100 feet; in a note of 55 vibrations, it will be 20 feet; in a note of 100 vibrations, it will be 11 feet.

A note *resonates* in a cylinder having the same length as the wave-length of vibrations which constitute the note, or having a length which is an exact divisor of the wave-length of the original note. If different notes are simultaneously sounded, a cylinder will resonate with and reinforce the note of corresponding wave-length, and that note will be heard louder than the accompanying notes. Similarly, tense strings and membranes will *resonate* with certain notes rather than with others, according as the vibration numbers of the notes do or do not correspond with the vibration number of the string or membrane when pulled or struck. A given note loudly sounded in front of a series of strings tuned to different notes, will set in vibration certain strings to the exclusion of others.

Overtones, or upper partial tones.—The principal or fundamental vibrations constituting a tone are usually accompanied by secondary tones, higher and of less intensity, which greatly affect its 'timbre.' A simple tone free from overtones is soft, weak and dull. The tone of an instrument giving overtones in the chord of that tone, is fuller, richer, and more sonorous than a simple tone. If the overtones are uneven, but not excessive, the musical character of the tone remains, and may be peculiarly agreeable, but if the uneven overtones are too marked, or too numerous, the tone is rendered rough or penetrating, and is no longer agreeable to a civilised ear.

Beats; undertones, differential, or beat-tones.—Two slightly different notes, sounding together, alternately strengthen and weaken each other by interference, and the succession of phases is audible as *beats*. A tuning-fork of 436 vibrations sounding with a tuning-fork of 440 gives 4 beats per second, *i.e.* the frequency of beats per second corresponds with the difference in the numbers. Beats, in sufficiently rapid succession, give rise to a secondary, differential, or beat-tone. Thus a tone of 132 vibrations with a tone of 198 vibrations gives a beat-tone of 66 per second. Widely different notes can also give beat-tones, the vibration frequencies of which will correspond with the 'positive' and 'negative' remainders obtained by dividing the vibration-frequency of one note by that of the other (König). Notes with vibration-frequencies of 110 and 440, sounding together, give no beat-tone, there being no remainder on dividing 440 by 110. Notes of 120 and 440 will give beat-tones with vibration-frequencies of 80 and 40.[1]

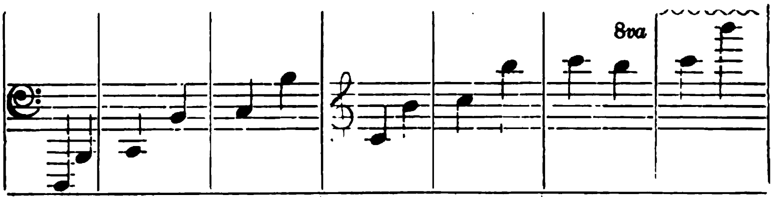
Tones are *concordant* when their vibration numbers bear to each other simple ratios, expressible by small whole numbers. Such tones harmonise and form concords or chords when sounding together. Tones are *discordant* when their vibration numbers do not bear to each other ratios as above. Such tones clash and form discords when sounding together.

In the major chord . .	C	E	G	c
the vibration numbers are	132	165	198	264
their ratios are	4	5	6	8

---

[1] 120 goes into 440 three times, leaving 80 as the *positive* remainder; or four times, all but 40, which is the *negative* remainder.

In the discord . . . . C D E
the vibration numbers are 132 148·5 165
and are not reducible to small whole numbers.



B,, $61\frac{7}{8}$ (60)	B, $123\frac{3}{4}$ (120)	B $247\frac{1}{2}$ (240)	*b* 495 (480)	*b*, 990 (960)	*b*,, 1980 (1920)	*b*,,, 3960 (3840)
A,, 55 (53·3)	A, 110 (106·6)	A 220 (213·3)	*a* 440 (426·6)	*a*, 880 (853·3)	*a*,, 1760 (1706·6)	*a*,,, 3520 (3413·3)
G,, $49\frac{1}{2}$ (48)	G, 99 (96)	G 198 (192)	*g* 396 (384)	*g*, 792 (768)	*g*,, 1584 (1536)	*g*,,, 3168 (3072)
F,, 44 (42)	F, 88 (85·3)	F 176 (170·6)	*f* 352 (341·3)	*f*, 704 (682·6)	*f*,, 1408 (1365·3)	*f*,,, 2816 (2730·6)
E,, $41\frac{1}{4}$ (40)	E, $82\frac{1}{2}$ (80)	E 165 (160)	*e* 330 (320)	*e*, 660 (640)	*e*,, 1320 (1280)	*e*,,, 2640 (2560)
D,, $37\frac{1}{8}$ (36)	D, $74\frac{1}{4}$ (72)	D $148\frac{1}{2}$ (144)	*d* 297 (288)	*d*, 594 (576)	*d*,, 1188 (1152)	*d*,,, 2376 (2304)
C,, 33 (32)	C, 66 (64)	C 132 (128) (8-foot organ-pipe)	*c* 264 (256) (middle *c*)	*c*, 528 (512) (standard tuning-fork)	*c*,, 1056 (1024)	*c*,,, 2112 (2048)

Musical notes and their vibration-frequencies. The numbers in parenthesis are such as would be obtained by taking the series C,, ... *c*,,, in successive powers of 2, viz. 2^5 . . . . 2^{11}.

In forming numerical estimates of auditory sensibility, it is necessary to remember:—(1) that the strength of sound made by a body allowed to drop upon a surface, is proportional to the square root of the height of drop; (2) that the strength of sound varies inversely as the distance squared between origin and ear; *e.g.* the strengths of sound made by a ball falling from heights 1, 4, 9, 16 are 1, 2, 3, 4; the strengths of a given sound at distances 1, 2, 3, 4 are 1, $\frac{1}{4}$, $\frac{1}{9}$, $\frac{1}{16}$.

HEARING

The organ of hearing is composed of: (I) a receptive part —the external, middle and internal ear; (II) a transmissive part, the auditory nerve; (III) a perceptive part, the cortex of the brain.

The ear.—Anatomically, the ear consists of: (1) The external ear, comprising the pinna and auditory meatus, by which in normal hearing, sonorous vibrations are conducted to and concentrated upon the tympanic membrane or drum which divides the internal from the middle ear. (2) The middle ear, or tympanum, containing a chain of small bones, the three auditory ossicles, malleus, incus, and stapes. (3) The internal ear, comprising the vestibule, cochlea, and semicircular canals, and containing the peripheral termination of the auditory nerve—the hair-cells of the organ of Corti.

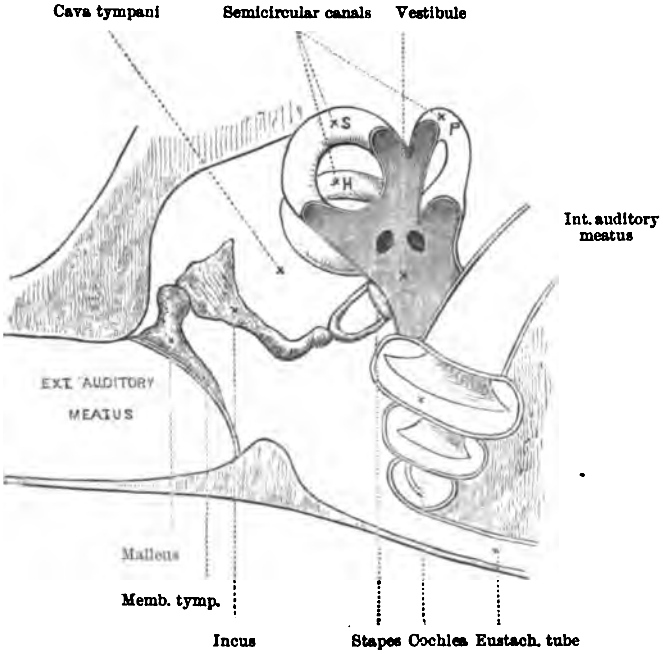


FIG. 240.—DIAGRAMMATIC VERTICAL SECTION THROUGH THE AUDITORY APPARATUS.

Sonorous vibrations concentrating themselves upon the membrana tympani, cause that membrane to vibrate, its vibrations are transmitted through the auditory ossicles to the fluid which fills the internal ear, and the vibrations of that fluid excite the peculiarly modified epithelium, from which the auditory nerve is the conducting channel to the brain.

The *membrana tympani* possesses a physical peculiarity distinguishing it from ordinary stretched membranes, which resonate with particular notes, inasmuch as it does not exhibit this physical preference to any marked degree, but vibrates with equal readiness to all kinds and tones of sound. It may, nevertheless, in some degree be attuned or accommodated to differences of pitch by means of the muscles which pull upon the auditory ossicles, and through the Eustachian tube by variations of air pressure.

The ossicles.—The vibrations of the membrane are transmitted along the ossicles, not merely as vibrations of sound are transmitted along solids, but as actual movements of the bones, acted upon and acting as levers. The movements are not molecular, but molar, and they have been observed and measured. The handle of the malleus attached to the membrana tympani forms one end of the lever—that to which the force is applied, the base of the stapes, attached to the membrane of the fenestra ovalis, forms the other end of the lever—that at which the force effects movement; the hinge or axis of rotation is in an antero-posterior line joining the points of attachment of the malleus and incus to the wall of the tympanic cavity. The relation between the two arms of this lever is such that the oscillation of the tympanic membrane is transmitted to the membrane of the fenestra ovalis with an amplitude diminished to two-thirds, and with corresponding mechanical advantage. The amplitude of movement of the tympanic membrane ranges from a maximum of $\frac{1}{10}$ mm. down to the immeasurably small; that of the stapes, from a maximum of $\frac{1}{15}$th mm., likewise down to the immeasurably small—or, to give some idea of how small—down to less than $\frac{1}{10000}$ μ.

The *tensor tympani* muscle, attached to the handle of the malleus, pulls the latter and with it the tympanic membrane directly inwards, thus tightening the membrane. It is served by the fifth nerve. With this movement the stapes is more closely applied to the fenestra ovalis and tilted forwards; amplitude of vibration is thus limited, and sounds, especially low notes, are consequently weakened. The *stapedius* muscle, attached to the neck of the stapes, tilts the latter backwards. It is served by the seventh nerve. Its influence upon the transmission of sound is not known.

The *Eustachian tube* establishes communication between the tympanic cavity and the pharynx, and thus admits atmospheric pressure to the cavity of the tympanum. It is probably not continuously open, but only so on more or less frequent occasions, *e.g.* during the act of swallowing. If it be obstructed, atmospheric pressure on the outside of the membrana tympani is not balanced by counter-pressure from the inside, the tympanic cavity becomes filled by exudation, and hearing is interfered with. Hardness of hearing from this cause is temporarily removed by inflation of the tympanum; this may be effected by a strong expiratory effort of the patient with mouth and nostrils closed; or the patient being directed to swallow, air may be forced through from the nostrils by an operator during the act of deglutition. Hearing is temporarily dulled whenever air-pressure within the tympanic cavity is less or greater than that upon the outer surface of the membrane; during a forcible inspiration or expiration with closed mouth and nostrils, sounds, especially low notes, are less distinctly heard than when tympanic air-pressure is normal, *i.e.* equal to atmospheric pressure.

Hearing viâ the cranium.—If, while the vibrations of a tuning-fork are dying away and have just become inaudible by the usual channel, the handle of the fork be applied to the teeth or skull, the sound will become again distinctly audible—*i.e.* the vibrations are transmitted by the skull. If, while the tone is being listened to in this manner, one ear be gently closed, the sound will be intensified on that side. A fully satisfactory explanation of this fact cannot be given; it was formerly supposed that the vibrations were transmitted by the bones of the skull directly to the internal ear; a sound *viâ* the cranium, more distinctly heard on one side (that side being defective to sounds reaching it by the usual channel) than on the other, was believed to indicate defect of the sound-conducting apparatus (tympanic membrane and ossicles). Both these suppositions have been disproved—the vibrations heard through the skull are transmitted by its bones to the membrana tympani and ossicles, and thus onwards to the internal ear, but they have not been proved to be directly transmitted to the internal ear better than through the middle ear, and they certainly do not directly excite either the auditory nerve or the auditory centre. Defects of the middle ear and of the internal ear alike interfere with the hearing of sounds *viâ* the cranium as well as *viâ* the meatus; if a person who is dull of hearing hears a tuning-fork on the cranium louder in that ear, he probably has a blocked meatus, and not a defect of the middle ear; if he had the latter, the tuning-fork would be less audible on that side.

The apparatus of the middle ear—membrana tympani and auditory ossicles—is useful, but not absolutely indispensable; hearing is greatly impaired by their destruction, but it is not by any means abolished, and slight perforations of the membrana are common without obvious hardness of hearing. Some small proportion of sound must therefore be transmissible through the cranium to the terminal apparatus of the internal ear.

Physiological anatomy of the internal ear.—The internal ear or labyrinth consists of the vestibule, the cochlea, and the three semicircular canals. Of all these parts the walls are bone, the lining is membrane, the contents are fluid (endolymph and perilymph), and a modified epithelium, which constitutes the commencement of the auditory nerve; otoliths and so-called 'sand,' composed of calcium carbonate, also form part of the contents of the labyrinth, but have no assignable function.

Functions of the internal ear.—As regards the *vestibule*, there are no facts to justify any dogmatic statement whatever; at the most we may regard as not impossible that its epithelium may be excitable by vibrations of the endolymph. As regards the *semicircular canals* we have reason to believe that they have to do with equilibration, and have quite dismissed the gratuitous supposition that they are concerned in the appreciation of the direction of sound. The *cochlea* is evidently the most highly specialised portion of the internal ear, its minute anatomy and its analogies with well-understood physical instruments, indicate with reasonable certainty that it constitutes the physiological receiver of sonorous vibrations—and there are a few physiological and pathological facts in additional support of this conclusion.

The cochlea contains the terminal apparatus of the auditory nerve. It consists essentially in a spiral tube of bone, 25 to 30 mm. long, lined by membrane, and divided by membranous partitions into three channels—*scala vestibuli*, *scala tympani*, and *canalis cochleæ*; the lamina spiralis ossea and the *membrana basilaris* divide the scala tympani from the scala vestibuli, and the membrane forms the floor of the canalis cochleæ, of which the roof is formed by the membrane of Reissner; the scala vestibuli commences at the fenestra ovalis and communicates with the scala tympani at the helicotrema; the scala tympani commences at the fenestra rotunda; the fenestra rotunda is covered by membrane; the fenestra ovalis is covered by the base of the stapes and its orbicular ligament, so that any vibration from the membrana tympani, transmitted along the ossicles, must pass through the entire length of the cochlea. The floor of the canalis cochleæ, or membrana basilaris, carries an avenue of cells which constitute the *organ of Corti*; this consists of a double row of stiff cells, the inner and outer rods of Corti, and of several rows of *hair cells*—a single rank of inner hair cells, and a border of outer hair cells two or three deep, into which the terminal filaments of nerve-fibres have been traced. The organ of Corti is covered by a thin reticulated or fenestrated membrane through which project the hairs of the hair cells, and by the free margin of a loose thick membrane, the *membrana tectoria*, which rests upon the organ; we shall find that it is of importance to recognise that the membrana basilaris is equivalent to a series of radial fibres stretching from the margin of the spiral lamina to the spiral ligament, and that the breadth of the membrane, *i.e.* the length of the fibres, increases from below upwards—at the base of the cochlea the breadth is 41 μ, at its apex, 495 μ.[1] The organ of

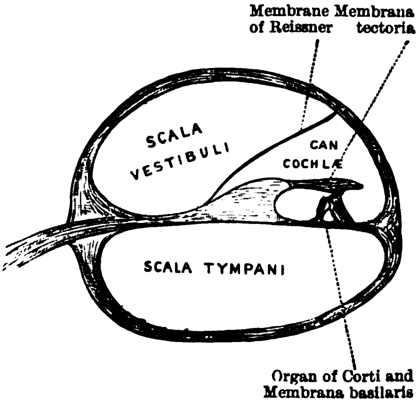


FIG. 241.—DIAGRAMMATIC TRANSVERSE SECTION THROUGH A TURN OF THE COCHLEA.

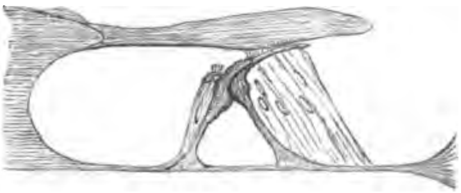


FIG. 242.

Diagram to show the position of the organ of Corti resting on the Membrana basilaris and covered by the Membrana tectoria. (N.B. No attempt is made to reproduce the exact anatomical features of the parts.)

---

[1] These are v. Hensen's figures. According to Retzius, the inequality of breadth is much smaller, viz. 0·36 mm. at apex, 0·21 mm. at base.

Corti of man has been estimated to include 3,000 pairs of rods and between 10,000 and 15,000 hair cells.

We have up to this point traced the path of sonorous vibrations through the external and middle ear, through the ossicles to the fenestra ovalis, and through the middle ear up the scala vestibuli, and down the scala tympani. We have now to examine the mechanism by which such vibrations may be supposed to effect auditory excitations.

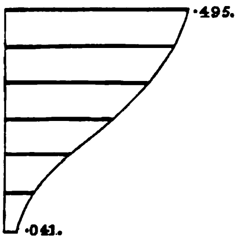


FIG. 243.

Diagram to show the manner in which the breadth of the membrana basilaris increases from below upwards. Total length 30 mm. Breadth × 50 increasing from ·041 mm. at the base to ·495 mm. at the helicotrema. (After Hensen's measurements.)

According to the theory of Helmholtz the stretched radial fibres of the basilar membrane behave towards the vibrations of the endolymph, as the strings of a piano towards vibrations of the air caused by different notes. Different strings in the piano vibrate with different notes, particular strings respond to particular notes, and in analogy with this known relation, it is supposed that different fibres in the basilar membrane vibrate with different notes, that particular fibres respond to particular notes. It is to be supposed that such responsive vibrations, although of infinitesimal magnitude, extend to the particular hair cells resting upon the membrane, and give rise to excitations, which, conducted along nerve-fibres to the brain, produce different auditory sensations. On this theory it is supposed that the basilar membrane and hair cells of Corti constitute an apparatus by which sound vibrations are analysed and differentiated at the periphery, and as a supplementary feature of this theory, partly based upon the increasing breadth of the basilar membrane from below upwards, partly upon direct experiments upon dogs, it has been stated that low notes set into sympathetic vibration the upper fibres, high notes the lower fibres, of the basilar membrane. This theory has received support from experiments on dogs, and from the observations of von Hensen on the 'auditory' sacs of crustacea. These organs contain, besides otoliths, epithelial cells bearing hair-like processes which range from 140 to 720 μ in length. Different notes were found to set in motion different groups of hairs, but loud notes were found to set in movement all the hairs. The experiments on dogs are not very numerous or convincing; it is difficult to limit a lesion of the cochlea to its base or to its apex, and no less difficult to determine whether a dog has suffered in his appreciation of high and low notes; to be at all convincing, a dog who previously howled in response to high and low pitched music alike, should after destruction of the top of the cochlea, respond only to high-pitched music, or, after destruction of the bottom of the cochlea, only to low-pitched music: this desideratum has not been fulfilled.

Rutherford in 1886 proposed an alternative theory in which the mechanism is compared with that of the telephone. He supposes that every cell of Corti is impressed by every audible vibration, and that the sound-wave transmitted by the fluid of the scala tympani through Reissner's membrane to the canalis cochleæ, impresses the membrana tectoria and sets in vibration all the hairs of Corti's cells. He considers that through the intervention of these cells the vibrations are translated into nerve-impulses, which correspond with them in frequency, amplitude, and form, 'just as in a telephone the sound-vibrations are translated by the iron plate and magnet into electrical movements which correspond to those of the sound received.' He objects to the Helmholtz-Hensen theory that a simple radial structure of the basilar membrane is by no means constant in all animals, that its increasing breadth from base to apex has been greatly over-estimated by Hensen, and that the probable consistence of the parts is not such as to suggest the occurrence of sympathetic vibration. According to Rutherford, complex vibrations are not analysed at the cochlea, but translated into corresponding complex nerve-impulses and sensations.

Hermann has recently published an experiment which is very unfavourable to the theory of consonation and peripheral sound analysis:—Two simultaneous tones $a_{,}$ (880) and $c_{,,}$ (1056) gave by the ear the beat-tone F (176); but it was not found possible to produce any such beat-tone in a distant resonator which was perfectly responsive to F as a simple tone.

A full consideration of the theories of auditory mechanism and of their respective merits would lead us too far; we may remark in conclusion of this difficult subject that the growth of evidence, so far from strengthening, has weakened the consonation theory. We may regard the basilar membrane as a long narrow drumhead, repeating the complex vibrations of the membrana tympani, and suppose that it vibrates in its entire area to all sounds—although more or less in some parts than in others—giving what we may designate as acoustic pressure-patterns between the membrana tectoria and the subjacent field of hair-cells. In place of an analysis by consonation of particular radial fibres, it may be imagined that varying combinations of sound give varying pressure-patterns comparable to the varying retinal images of external objects.

There remains for us to trace the excitations made in one or other of the above ways from their origin in the organ of Corti to their terminus in the cerebral cortex. The cochlear nerve-fibres (medullated and of small calibre) are anatomically traceable to the spinal bulb by the dorsal root of the eighth nerve to the principal auditory nucleus and through the accessory auditory nucleus. From this station they doubtless proceed to the cortex cerebri, though along what precise paths, and to what precise region, it is not possible to say with assurance. It is, therefore, with considerable reserve that statements may be quoted to the effect that auditory channels pass to the corpus geniculatum posterum (testis) of the opposite side, and thence to the cortex of the first temporal gyrus. The last assertion in particular we shall find to be very unassured when we come to the study of cortical localisation.

Estimates of pitch and of intensity of sound are the effect of cerebral comparisons with previous experience. The estimate of direction is mainly formed by inference from the differing intensities of the acoustic impressions on the two sides; a blindfolded person with the head kept stationary can easily localise correctly the direction of a sound produced to the right or left of the auditory field, but is very liable to misjudge the direction of sound directly in front or directly behind; he will easily localise correctly by moving the head to one side or the other.

The range of vibration frequency within which tones are audible as such is from about 30 to 30,000 per second; but individual variations of auditory sensibility are considerable—of many persons the highest audible limit is 20,000, of others, 15,000 or even less. According to Exner, two sounds can be recognised to be distinct, if the interval between them is not less than 0·002 sec. According to Schafhäutl, a person of acute hearing can detect the sound made by a cork ball weighing 0·001 grm. falling from a height of 1 mm. on a glass plate 91 mm. distant from the ear.

TASTE, SMELL, AND CUTANEOUS SENSATION. THE MUSCULAR SENSE

Taste and **smell**, although included under the classical five senses, and playing an important part in the selection of food-stuffs, are from an experimental point of view of very subordinate interest.

The principal nerve of taste is the glosso-pharyngeal, which supplies the posterior part of the tongue, *i.e.* that portion of the buccal surface which most contributes to taste. Two other nerves also take part in taste, inasmuch as their integrity seems to be necessary to the process; these are the so-called gustatory branch of the 5th, which is a common sensory nerve, and the chorda tympani of the 7th, the mode of action of which upon taste is, however, imperfectly understood. Sweets and bitters are best tasted when applied to the back of the tongue; salts, acids, and alkalies can be equally well 'tasted' by its lateral or anterior portions.

Smell is more important in its contribution to 'taste' than to smell proper. Taste is in reality in large measure effected by aroma. If smell is lost, or temporarily suppressed by filling the nostrils with fluid, very little discrimination by taste alone is left to us; most of our 'tasting' is by nose.

The nerve-ends by which taste excitations are considered to be received are the *taste-bulbs*, which are most prominently distributed along the side of the trenches round the circumvallate papillæ, and which, in the rabbit, occupy the parallel trenches of two oval patches at the postero-lateral parts of the tongue. Each taste-bulb is an oval body formed of long fusiform cells, arranged in cortical and medullary groups; the latter, into one pole of which nerve-fibres have been traced, project through an opening left at the opposite pole between the cortical cells.

The epithelium of that portion of the nasal mucous membrane to which the olfactory nerve-fibres are distributed has been termed the olfactory epithelium. It is composed of non-ciliated columnar cells, among which are scattered narrow, rod-like, 'olfactory cells' with large oval nuclei.

Cutaneous sensibility includes common sensation, and is sometimes classed as or with a special sense—that of *touch*; it is by means of cutaneous impressions that we are made conscious of the consistence, texture, and temperature of external objects, and it is partly by cutaneous sensation, partly by muscular sensation that we ascertain and compare their weight. As tactile organs, the skin of the palm of the hand and that of the sole of the foot play a most important part in our guidance: the varying pressures of the body on the plantar surface guide equilibration and locomotion; we touch or feel objects by means of the hand and finger tips, and we consciously utilise the sensations so acquired in our knowledge of objects and in our skilled movements.

The two most noteworthy subjects in connection with cutaneous sensibility are:—(1) its differences at different parts as ascertained by Weber's compass method; (2) the question of specific 'heat nerves,' and 'cold nerves,' as investigated by Blix and by Goldscheider.

The nerve-ends to which tactile function is attributed are the touch corpuscles of Wagner, which in the specially tactile area, *e.g.* the finger tips, are set in ranks occupying rows of papillæ beneath the edges of the skin, forming thus what may be collectively regarded as a tactile organ. Each touch corpuscle is a small oval glomerulus, 50 to 200 μ long, formed of the branched and tangled ends of a medullated nerve-fibre, held together and surrounded by connective tissue. They are unequally distributed over the surface of the body, being numerous and crowded at the tips of the fingers, few and scattered on the arms, legs, and trunk. Our discriminative tactile power is far greater by the tips of the fingers than by the skin of the back, and varies between these two extremes in various other portions of the surface. A measure of this discriminative power is obtained by finding the greatest distance at which two points of a pair of compasses applied to the skin are felt single, or the smallest distance at which they are felt double. Tested by this method (Weber's), the following are some average values in millimeters:—

Side and dorsum of tongue	9	Forearm (front)	15
Tip of tongue	1	Forearm (back)	45
Palmar surface of hand	8	Neck, back, arm, thigh	50 to 70
Palmar surface of hand, terminal phalanx	2	Cheek	15
Palmar surface of hand, middle phalanx	4	Lip (white)	9
Palmar surface of hand, proximal phalanx	5	Lip (red)	4·5
Dorsal surface of hand	30	Lip, inner surface	20
		Forehead	22·6
		Occiput	27·1

By minute investigation of the skin, supplemented by subjective introspection, some remarkable conclusions have been arrived at, viz. that the skin contains many kinds of nerve-fibres and end-organs, separately subserving impressions of pressure, of pain, and of temperature. Of these investigations the most noteworthy is that of Goldscheider, to the effect that different spots of skin are respectively excitable by heat and by cold, and that the nerve-fibres leading off from such 'cold' spots and 'heat' spots are specifically different from each other, as well as from the nerve-fibres leading off from 'pressure-spots,' and from 'pain-spots,' in accordance with the law of specific nervous energies.

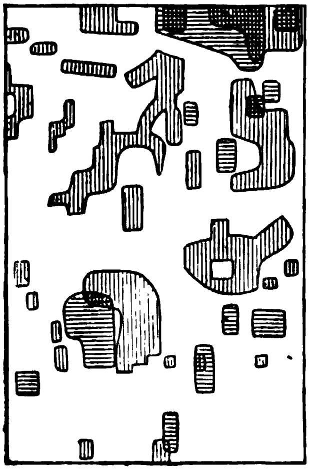


FIG. 244.

Cutaneous 'cold' spots (vertical shading) and 'hot' spots (horizontal shading); anterior surface of the thigh. (Goldscheider.)

The **muscular sense** is a convenient name for a property the actual mechanism of which is very indefinite, although many phenomena may reasonably be referred to it.

We are informed of the position of our limbs partly by the state of the skin, partly by the state of the muscles, and, seeing that muscle—or, properly speaking, tendon and fascia—possess afferent nerves, we have some right to assume that the sense of effort which we feel is in part at least obtained through such channels, *i.e.* that we have a true muscular sense. We estimate weight and difference of weight chiefly by means of trial efforts, by which we ascertain how much our muscles must be contracted in order to lift the weights, and we may reasonably suppose that the amount of contraction is estimated by a muscular sense. But this property in the form of centripetal process from muscle is not supported by any direct proof, and does not exclude an alternative or complementary supposition to the effect that the muscular sense is a central consciousness of outgoing effort—a feeling of expended energy in 'motor' centres (Wundt, Bain).

Among the numerous natural groups of movements which enter into the motor conduct of the body, those of equilibration and of locomotion especially attract attention by their universal importance and constant necessity. They are reflex adjustments to peripheral sensations—visual, labyrinthine, cutaneous, and muscular; and there is a disposition to regard these adjustments as being reflex in more *detailed* manner than other groups of co-ordinate movements, such as those of speech, or of writing, or of special crafts. It is considered that the state of tone and of contraction is, item by item, in direct reflex response to peripheral muscular tension, exciting a muscular sense by the channels of afferent nerves from the muscles themselves, or from their tendons, or from the articulating surfaces. This may be so, but it is not proved; it is not even probable. No doubt reflex adjustments are continually ebbing and flowing in the maintenance or alterations of muscular attitude, and the existence of a reflex 'tonus,' if not conclusively proved, is highly probable. But the assumption that in a series of movements each individual movement is a reflex spinal response to a pull of the muscle, or of the tendon, is inadmissible; in the large slow movements of locomotion, and still more in the small rapid movements of vocalisation, we must suppose that the constituent items in the co-ordinate series are measured out in due proportion and sequence in the emissive organ, independently of discrete peripheral calls through 'muscular sense.' There are also reasons for admitting that a direct peripheral response of muscle to extensile stimuli contributes to that harmonised action of antagonistic muscles which insures their smooth and steady service (*v.* p. 341).

Bearing these points in mind we are free to recognise the great importance of central guidance by peripheral conditions. A normal man walking perfectly with his eyes open, with a normal state of his plantar touch organ, and with a normal sensory innervation of his motor organs (muscles, tendons, ligaments and articular surfaces) will walk less or more imperfectly if one or more of these sources of information is perturbed or lost. But this is not all. In the co-ordinate function of any synergic group of muscles at least three conditions must be fulfilled—(1) impulses must be emitted from the centre in appropriate manner and degree; (2) the muscles must be 'in touch' with the spinal axis, duly responsive to the reflex ebb and flow arising from altering peripheral states; (3) they must be in touch with each other, directly reacting against that passive extension which antagonist muscles undergo from each other. If the first condition be at fault, the result is a disorder of movement, of which 'stammering' is the type; if the second or third are out of measure (and they are so closely associated as usually to go right or wrong together) we witness 'ataxic' effects, of which locomotor ataxy is the most familiar and extreme example.

The nerves from the vestibule and semicircular canals form the vestibular nerve (medullated fibres of large calibre), which is anatomically traceable to the lateral portion of the auditory nucleus in the spinal bulb by the ventral root of the eighth nerve. From this station onwards the destination of the nerve is not so clear; tracts from the nucleus are said to pass to the cerebellum by way of the restiform body. The principal end-organ of the vestibular nerve is formed by the bristle-cells of the so-called 'acoustic' crests of the ampullæ. They are probably not auditory in function, but 'equilibratory'—*i.e.* they are the origin of sensations which are caused by pressure effects of the endolymph in the ampullæ, and which contribute to the maintenance of normal muscular equilibrium. The directions of the three semicircular canals are very nearly in those of the three dimensions of space, and the planes occupied by the six canals are approximately as indicated in the diagram. Thus a rotation of the head clock-wise would give rise to greater pressure of endolymph in the ampulla of the right horizontal canal; a sudden cessation or reversal of rotation would give greater pressure in the ampulla of the left horizontal canal (Crum Brown). Clinical records are appealed to in support of the view that the integrity of the semicircular canals is essential to equilibration. 'Menière's disease' has as its prominent features deafness, giddiness, and staggering, presumably due to irritative lesion of the internal ear. And we shall see in a later section (p. 509) that among the experimental causes of forced movements, excitation of the semicircular canals plays a prominent part. On the other hand it should be mentioned that most careful experiments made on cartilaginous fishes have failed to demonstrate any connection between the semicircular canals and the co-ordination of movements. (Sewall, Steiner.)

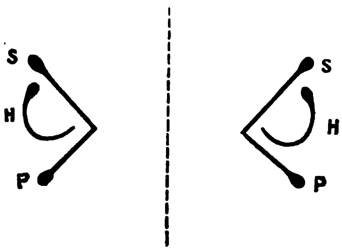


FIG. 245.

Diagrammatic horizontal section through the head to illustrate the planes occupied by the semicircular canals.

CHAPTER XIV

THE SPINAL CORD AND BULB

468 **Physiological anatomy:** White and grey matter—Nerve-fibres and nerve-cells—White columns and vesicular columns—Segmental centres.
474 **The spinal cord as a conductor:** Nerve-roots—Their functions—Effects of section and of excitation—Recurrent sensory fibres.
475 **Paths of motor and of sensory impulses:** Three kinds of data—experimental, pathological, and developmental—Complete transverse division—Hemisection—Longitudinal division—Two hemisections—Tracts of degeneration—Development—Further experiments.
478 Direct excitability of spinal cord—Stenson's experiment—Functional excitability—Rate of conduction.
483 **The spinal cord as a centre:** Reflex action—Automatic action—Psychical action—Summation of stimuli—Diffusion of stimuli—Inhibition of stimuli. Time of reflex action.
  Effects of strychnia—Tetanus—Clonus—'All or nothing'—Diffusion—Lost time.
488 **Centres of the spinal cord and bulb:** The general notion of special centres—Their enumeration.

THE CRANIAL OR BULBAR NERVES

496 Their bulbar nuclei of origin—Summary of their functions.
501 **The sympathetic 'system':** Its origin from the spinal cord and bulb.

The spinal cord and bulb. *Structure.*—The spinal cord consists anatomically of *white* matter and of *grey* matter; histologically the white matter is chiefly composed of nerve-fibres; the grey matter is chiefly composed of nerve-cells and of nerve-fibrils; physiologically the spinal cord is a *nerve-centre* by virtue of the cells of the grey matter, a *conductor* of nervous impulses by virtue of the nerve-fibres of the white matter, and in less degree possibly by virtue of the nerve-fibrils of the grey matter.

Nerve-fibres in the white matter are medullated, vary greatly in diameter, and have no sheath of Schwann. Small fibres (5 μ) predominate in the posterior columns, large fibres (15 μ) in the cerebellar tract. Nerve-fibrils in the grey matter are for the most part the axis-cylinders of nerve-fibres and the branching processes of nerve-cells. Nerve-cells in the grey matter vary greatly in size; 'large' cells (60 to 130 μ in diameter) are most numerous in its anterior parts, and are connected with nerve-fibres of the anterior roots of the spinal nerves; 'small' scattered cells (20 μ in diameter) in the posterior parts of the grey matter are probably connected with nerve-fibres of the posterior roots of the spinal nerves. The supporting tissue in which the true nervous elements are embedded is called the *neuroglia*; it is of a fine fibro-cellular structure resembling adenoid tissue, but, chiefly on account of its resistance to artificial digestion, it is classed with keratin, and supposed to have originated from the epiblast. It persists in greatest abundance in the *substantia gelatinosa* which surrounds the central canal of the cord, and caps the tip of the posterior cornu. The central canal itself preserves through life a permanent vestige of its original formation by an infolding of the epiblast, in the form of a lining of ciliated epithelium. Nerve-cells and nerve-fibres are accumulated into longitudinal groups and strands, forming the various columns of the cord; strands of fibres form the *white columns*, longitudinal groups of cells form the *vesicular columns*. Grooves or fissures divide the white columns more or less superficially from each other into anterior, posterior, and lateral[1]

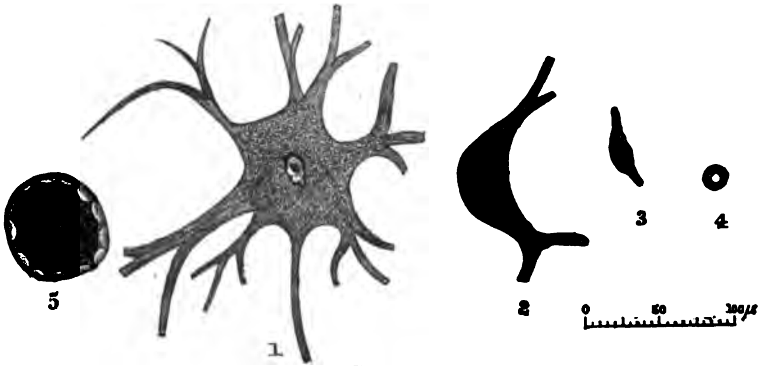


FIG. 246.

1. Cell of ant. cornu. 2. Cell of Clarke's column. 3. 'Solitary' cell of post. cornu. 4. Large nerve-fibre. 5. Cell of post. root ganglion. Drawn to the same scale, viz. × 200 diameters.

---

[1] The term 'lateral' is here used in its original anatomical sense, and is comprehensive of the pyramidal and cerebellar tracts as well as of the 'lateral columns' of neurologists.

columns. The relative situation of these several parts will be best understood by studying them in a transverse section (fig. 247), and an idea of their longitudinal extension may be gathered from the diagram given in fig. 248. The white columns and the anterior vesicular groups extend through the whole length of the cord, and the latter are most prominent in the cervical and lumbar enlargements, the spinal centres from which the great nerves of the anterior and posterior extremities respectively take origin. The intermedio-lateral or lateral tract and the postero-median group of cells, known as Clarke's posterior column, are elongated islands rather than continuous columns of cells. They have their greatest development in the thoracic region, in which the anterior columns of cells are most scanty; in this region Clarke's column forms what is known as the *dorsal nucleus.* Similarly situated islands of cells are found in the cervical and in the sacral regions, known as the cervical nucleus and as Stilling's sacral nucleus. In the upper cervical region the lateral nucleus forms the nucleus of origin of the spinal accessory nerve; in the bulb it is represented by the antero-lateral nucleus (=the chief vaso-motor centrè ?).

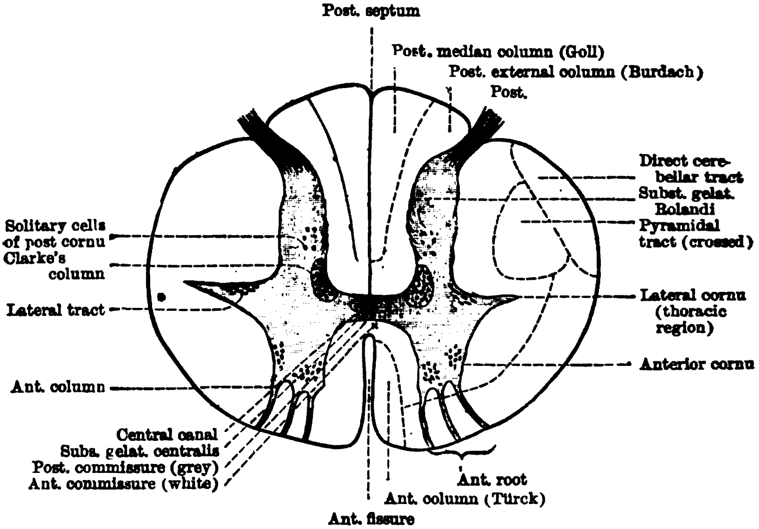


FIG. 247.—DIAGRAMMATIC TRANSVERSE SECTION OF THE SPINAL CORD. × 6 on a level with the eighth thoracic nerve. (After Schwalbe.)

At the bulb, in consequence of the opening out of the central canal into the fourth ventricle, and of the pyramidal decussation, the columns of the cord diverge and interlace, and its central grey axis is broken up into scattered nuclei of grey matter forming the medullary reticulum and insular nuclei; these last coming close to the posterior aspect of the bulb. Among them are to be distinguished the vagus and hypoglossal nuclei and the antero-lateral nucleus.

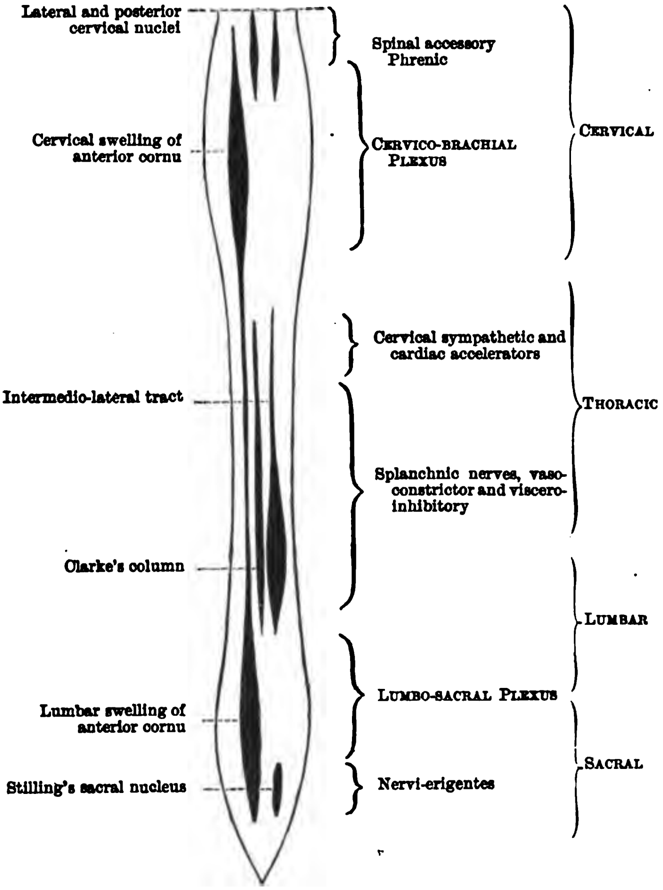

Lateral and posterior cervical nuclei
Spinal accessory
Phrenic
Cervical swelling of anterior cornu
CERVICO-BRACHIAL PLEXUS
CERVICAL
Cervical sympathetic and cardiac accelerators
Intermedio-lateral tract
THORACIC
Splanchnic nerves, vaso-constrictor and viscero-inhibitory
Clarke's column
LUMBAR
LUMBO-SACRAL PLEXUS
Lumbar swelling of anterior cornu
SACRAL
Stilling's sacral nucleus
Nervi-erigentes

FIG. 248.—SIDE-VIEW OF AN IDEAL LONGITUDINAL SECTION OF THE SPINAL CORD.

To illustrate the distribution of the vesicular columns. The levels of origin of the principal nerves are indicated by brackets.

Functions.—That the spinal cord as a whole is a nervous *centre* admits of very simple proof, both on the lower and on the higher animals and on man. A decapitated frog having lost brain and bulb, reacts by movements when the skin is pinched, and no longer so reacts when the spinal cord is destroyed. A man whose spinal cord is cut, say in the dorsal region, by disease or by mechanical injury, reacts by movements of his lower limbs when the soles of his feet are touched, and he bears witness to the fact that he feels nothing, that he is not conscious of any impression, *i.e.* that the reaction of the spinal cord is carried out without sensation. Such reactions are instances of reflex action in the original and restricted sense of

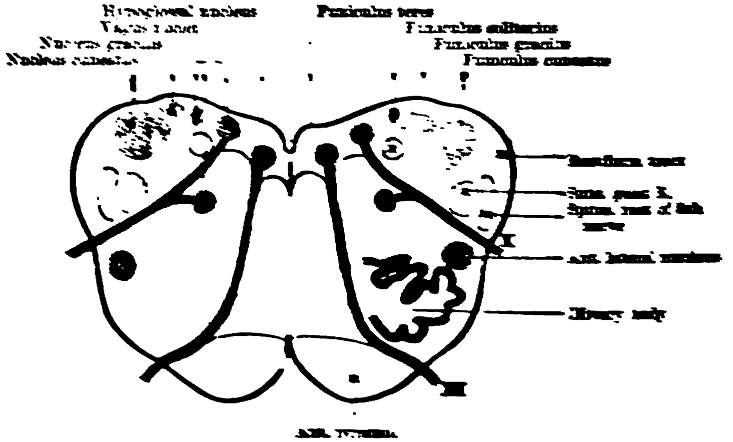


Fig. [illegible].—Transverse section of the spinal bulb at about the middle of the olivary body, to illustrate the principal nuclei and tracts of this area. (After Schwalbe.)

the expression: they are simple, immediate, local and unfelt responses to direct peripheral stimuli.

Injury or disease of transverse slices of the cord interferes with these reactions in definite transverse slices of the body: disease or injury of the cervical region abolishes reactions to and from the upper limbs, while reactions to and from the lower limbs may be unaffected; disease or injury of the lumbar region abolishes reactions to and from the lower limbs, while reactions to and from the upper limbs remain intact. This segmentation of spinal function applies to all vertebrate animals from man downwards. It is illustrated clinically by the various symptoms which characterise inflammation of the cord, when such inflammation [illegible] disease, or severance, or when it progresses [illegible] and it may [illegible] be experimentally recognised on a decapitated frog by dividing the cord in the mid-dorsal region, when it will be found that reflex action can be obtained from leg to leg, or from arm to arm, but not from leg to arm, or from arm to leg.

The grey matter of the cord is thus to be regarded as a series of *segmental centres* fused together into a continuous longitudinal mass, each centre giving off a pair of spinal nerves to the two symmetrical halves of a vertebral segment. In correspondence with this view we may expect to find that the amount of grey matter is greatest on a level with greatest development of the vertebral segments, *i.e.* on a level with the limbs. This indeed is the case to such an extent as to give considerable swellings of the grey matter with which the large nerves of the upper and lower limbs are connected; and even in the cords of animals which show no such swellings, we find that the number of cells is greatest at points whence large nerves take origin.

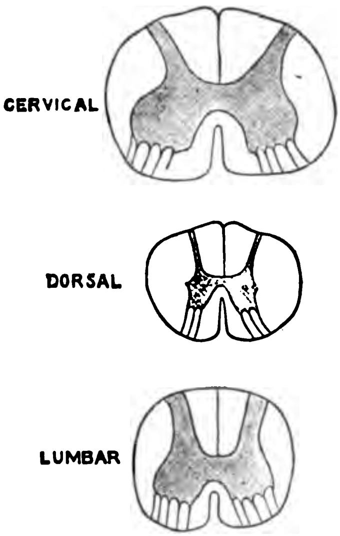


FIG. 250.—OUTLINE-SKETCH OF THREE SECTIONS (× 3).

Taken from the cervical, thoracic and lumbar regions of spinal cord (human).

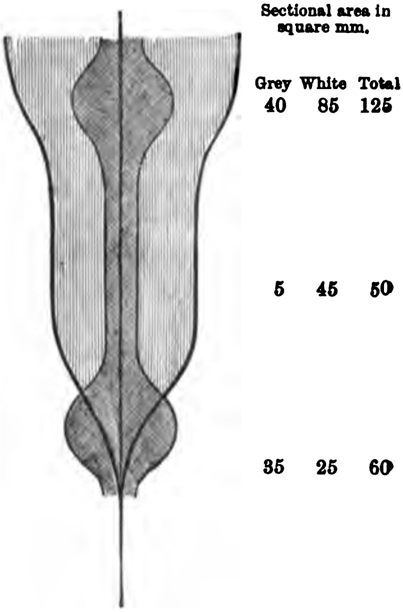


FIG. 251.—DIAGRAM-SKETCH BASED ON STILLING'S MEASUREMENTS.

To illustrate the area of white and of grey matter at different levels.

The spinal cord is also a *conductor* of nerve impulses. The white matter of the cord is in this respect to be regarded as a collection of nerve-fibres establishing connection between the brain and the grey matter of the spinal cord; the amount of white matter diminishes from above downwards progressively with the smaller number of spinal cells that remain to be reached by such fibres; thus at its upper part the white matter contains fibres sufficiently numerous to supply all the cells below, at a lower level it still contains fibres sufficiently numerous to supply all the cells below this level, but the number of cells in the latter case is smaller than in the former, and the number of fibres thus diminishes downwards. It is on this account, and not because they lose fibres into each pair of spinal nerves, that the white columns taper downwards.

There are reasons for accepting as highly probable, that there are no direct fibres between the cortex cerebri and the periphery (sensory or motor), *i.e.* no fibres to or from the cortex which have not a spinal cell in their course. Grounds for these statements are furnished (1) by actual enumeration of fibres and of cells throughout the spinal cord of a small animal—a laborious task, which has been undertaken in the case of the frog only; (2) by tracts of degeneration, *i.e.* 'descending' degeneration of the pyramidal tracts tapers downwards, and does not extend beyond anterior nerve-cells into motor nerves; 'ascending' degeneration of Goll's column is not traceable beyond the bulb (nucleus gracilis).

Nerve-roots.—Afferent and efferent fibres are intermingled in mixed nerves; in the roots of the spinal nerves they are separated, the anterior roots being composed of efferent or motor fibres, the posterior roots being composed of afferent or sensory fibres. Section of the anterior roots causes paralysis of motion; section of the posterior roots causes paralysis of sensation; excitation of the central end of a divided anterior root gives no effect, excitation of its peripheral end causes muscular contraction; excitation of the central end of a divided posterior root causes reflex movements, excitation of its peripheral end has no effect. One of these four statements requires qualification—excitation of the peripheral end of a divided anterior root, if the test be applied after the 'shock' caused by the preparatory operation has passed off, will evoke reflex as well as direct movements; the anterior root, although mainly composed of motor fibres, contains a few sensory fibres derived from the posterior roots, and therefore termed recurrent sensory fibres. All these facts, inclusive of those dependent upon the existence of recurrent sensory fibres, were discovered by Magendie (1822). Charles Bell (1811), to whom they are commonly ascribed, observed motion on excitation of the anterior roots of a recently killed animal, and inferred that the anterior or 'cerebral' roots are motor and sensory, and that the posterior or 'cerebellar' roots 'serve to govern vital actions.' A. Walker (1809) made the unfortunate guess that the anterior roots were sensory and the posterior motor.

Impulses along recurrent sensory fibres must run a very exceptional and often tortuous course; the fibres do not, as was first supposed by Magendie, turn back close to the junction of the roots, but they run in the nerve trunks towards, and even into the peripheral plexus of nerves, whence they return to the posterior roots (Bernard). It is probably owing to the excitation of recurrent sensory fibres that the excitation of the *peripheral*[1] ends of many nerves—motor as well as sensory (*e.g.* fifth and seventh)—is found to produce manifestations of pain, and that sensation, temporarily abolished by 'shock,' can reappear a day or two after nerve section (*e.g.* of the median nerve) without it being necessary to invoke any sudden reunion of the divided nerve.

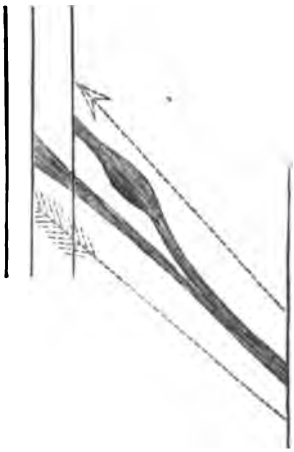


FIG. 252.—RECURRENT SENSORY FIBRES.

The probable course of impulse along them indicated by the dotted arrow; their degeneration occurs 'against' the arrow, their trophic centre being the posterior root-ganglion.

Paths of motor and of sensory impulses in the spinal cord.—A paralysis of motion or of sensation, caused by a lesion on one side of the brain, is on the side of the body opposite to the lesion. This connection, which is practically constant, proves that motor and sensory paths must cross the middle line. Where do these channels cross, and how far can we precisely define them? We shall find that this question can be answered with an approach to certainty as regards motor paths, but with far less assurance as regards sensory paths. Data from three different sources contribute to our knowledge of the matter :—(1) data obtained after experimental lesions upon animals, or accidental lesions upon man; (2) data obtained by the study of tracts along which degeneration is traced some time after the occurrence of such lesions; (3) data obtained by the study of the order of development of various tracts.

---

[1] The peripheral end of a divided nerve is the end attached to the periphery, the central end is that attached to the centre.

(1) **Experiments.**—The effect of complete transverse division of the cord is *paraplegia*, *i.e.* paralysis of voluntary motion and of sensation in all parts below the injury. The effect of hemisection, *i.e.* of transverse division of one half of the cord, is paralysis of voluntary motion on the same side with weakness on the opposite side, and paralysis of sensation on the opposite (?) side. Sensibility has been found exaggerated on the same side; by other observers it has been found that the loss of sensibility is greatest on the same side. The effect of longitudinal division in the middle line is said to be an abolition of sensation on both sides, and a weakness of movement not amounting to complete paralysis. The effect of two transverse hemisections on opposite halves of the cord, varies according to the interval between them; if near together, two hemisections are equivalent to a complete transverse division; if far apart, motility and sensibility are more or less preserved.

The generally quoted conclusions from these experiments are that motor channels cross at the *bulb*, sensory channels in the *cord*. Both statements must be qualified, and we may say at once that whereas precision will be added to the first statement, reservations to the second must be made almost amounting to contradiction. With regard to *motor* channels, while their major part cross at the decussation of the pyramids, a minor part (in man) cross in the spinal cord, and we shall see that these parts are picked out by degeneration, as well as recognisable by their tardy development, as the crossed and direct pyramidal tracts. But with regard to *sensory* channels the evidence is far more uncertain and unfinished. Clinical evidence shows that the sensory path crosses somewhere, but not where; until recently the statement was repeated unchallenged, and by mere force of repetition acquired perhaps undue credit, to the effect that sensory channels cross in the cord. Now, however, there is an increasing disposition to correct this view; the recent experiments of Gotch and Horsley and those of Mott have yielded evidence in opposition—the electrical token of centripetal impulses has been found most pronounced on the *same* side of the cord as excitation; monkeys after hemisection have been found with the less sensitive leg on the *same* side as the lesion, as was originally stated by Galen 1700 years ago, presumably from experiments on monkeys.[1] To such opposition evidence must also be added the indirect testimony of degeneration—'ascending' degenerations above a hemisection are most marked on the same side of the cord. We seem, in fact, to be approaching the conclusion that sensory as well as motor channels have their major decussation in the bulb, their minor decussation in the cord; in which case we must admit that sensory impulses from each side of the body can pass up both sides of the cord, but most on the same side.

The older experiments above alluded to originate from the Paris school, and are due chiefly to Brown-Séquard, who, however, no longer upholds the significance which has been attributed to them. More detailed experiments on the same subject have been made in Germany by Schiff, Türck, Stilling, Müller, and by Ludwig's pupils. The main result of these last was to the effect that the lateral columns of the cord are the chief channels of motion and of sensation, and that the anterior columns take part in motor conduction; vaso-motor, among other motor effects, were shown to have their passage in the lateral columns of the cord and in the anterior roots of the spinal nerves; after hemisection of the cord the vessels were found to be dilated on the same side below the injury.

Attempts have been made to further define what kinds of motion and of sensation pass along the various columns. Separate tracts have been assigned to *voluntary*, as distinguished from automatic or reflex motion, and although we must not hastily admit special and exclusive functions of particular strands, we may recognise the pyramidal tracts as pre-eminently the channel of 'voluntary' action; they are more voluminous in man than in any other of the mammalia. Separate tracts have been assigned to various modes of sensation. 'Tactile sensibility' has been billeted upon the posterior columns, 'sensations of pain' have been considered to be received through the grey matter, common sensation through the lateral columns, thermic sense and muscular sense through the posterior columns. All these opinions are mainly based upon the shifting ground of subjective interpretations, and are therefore most doubtful and inconclusive. Signs of sensation are difficult to read in animals, signs of lost sensations are even more equivocal, and observations as to whether different kinds of sensation are preserved or lost or altered, are particularly liable to be guided by the expectations of the observer.

---

[1] '. . . Moreover you have seen that transverse incisions of the whole cord deprive all parts of the body situated below of sensibility and of movement. . . . And you have seen in dissections that transverse incisions of the cord (from right to left or from left to right) which stop at its centre, do not paralyse all the inferior parts, but only the parts situated directly below the incision—on the right, when the right side of the cord has been cut; on the left, when it is the other side.' (Galen, 'X. Of the Parts Affected,' lib. iii. cap. xiv

Direct excitability of the spinal cord.—It might be expected that direct excitation of various tracts of the cord should be capable of yielding information concerning the different paths followed by nervous impulses. But this has not been found to be the case, the exact localisation of experimental stimuli is extremely difficult to accomplish on the intact cord, and to artificially isolate longitudinal tracts with the knife depresses excitability to such an extent that it may then with difficulty be manifested even with strong stimuli. It is for these reasons that diametrically opposed answers have been given to the question, 'Is the spinal cord excitable by direct experimental stimuli?' Van Deen, Schiff and Chauveau answered 'No.' Vulpian, Fick, and Dittmar answered 'Yes.' In the attempt to form our opinion from such conflicting statements of fact, we must bear in mind (1) that the excitability of the cord is easily depressed by the shock of the operation necessary to expose it; (2) that the cord is of complex structure, being composed of (*a*) nerve-fibres of the anterior and posterior roots; (*b*) nerve-fibres of the white columns; (*c*) grey matter; and the question must therefore be put separately to each of these three constituents. The nerve-fibres of the anterior and posterior roots pass obliquely through the white columns for a short distance above and below the level at which they emerge; the excitability of these root-fibres is admitted by all observers. By those who deny the direct excitability of the white columns, the muscular contractions which have been observed to ensue upon mechanical or electrical stimulation of the columns are attributed to stimulation of these root-fibres. The nerve-fibres of the white columns are admitted to give passage to nerve impulses between brain and cord; it is difficult to admit their inexcitability to direct stimulation, and it is very probable that their frequent failure to give evidence of direct excitability has been due to shock. The evidence required to prove the negative proposition is in this case far greater than that required to prove the opposite positive proposition.

An experiment of Fick's, which has been repeated by other experimenters, furnishes such evidence with regard to motor columns. By longitudinal incisions he isolated long strips of white matter, and in favourable cases obtained contractions as the result of excitations applied far from the point of division. Under these circumstances the stimulus was localised to the columns, and could not affect root-fibres which were cut. We may, therefore, admit the excitability of the white columns as proved, though it has been difficult of proof.

To test the direct excitability of the grey matter is a still more difficult task. That it can transmit motor and sensory impulses is admitted on all hands. That it is excitable by direct experimental stimulation cannot be asserted, fact in hand, for it occupies a central situation surrounded by nerve-fibres in close proximity. The fact is not proven. We may, however, remember that the grey matter of the cerebral cortex which is accessible, was long supposed to be inexcitable by direct stimuli, but is now generally admitted to possess direct excitability; the fact is, therefore, probable.

Excitability by experimental stimulation is not to be confounded with indirect or functional excitability evoked by stimuli which reach the cord by the natural channels. In this sense it is obvious that the cord (both white and grey matter) is excitable. A classical experiment of Stenson's demonstrates how rapidly the functional excitability of the grey matter is lost when the blood supply is arrested. The abdominal aorta in the rabbit can be completely compressed so as to arrest circulation in the lumbar part of the cord; if this arrest be maintained for two to three minutes, the posterior extremities become completely paralysed as regards sensation, voluntary motion, and reflex motion; the nerves and muscles are not paralysed, but the grey matter of the cord is rendered inexcitable. The experiment furnishes one among other proofs that motor and sensory channels all pass to and from the brain *viâ* a station of grey matter in the cord, and that there are no direct channels of white matter in either direction between the brain and the periphery. Arrest of circulation for so brief a period, though sufficient to abolish the excitability of nerve-cells, is not sufficient to abolish the conductivity of nerve-fibres.

The same fact is demonstrable on decapitated animals. Excitation applied by means of electrodes inserted into the vertebral canal a minute or two after decapitation, gives contractions of the upper extremities (by direct excitation of motor nerve-fibres), but no contraction of the lower extremities, because conduction is interrupted by inexcitable grey matter.

(2) **Degenerations.**—After transverse division of the cord, either experimentally upon animals or accidentally upon man—*e.g.* in the mid-dorsal region—degenerations occur along certain tracts above and below the seat of division; the former—called 'ascending'—are found in the column of Goll and in the cerebellar tract; the latter—called 'descending'—are found in the column of Türck and in the lateral column. A complete transverse division of the cord gives, of course, no information whether or no degenerated tracts cross the middle line; hemisections, or unilateral lesions, are necessary to supply such information. As regards descending degeneration, however, abundant data are furnished by cases of cerebral hemiplegia, where, in consequence of a brain lesion, a definite tract of fibres degenerates and can be traced in the brain, in the bulb, and in the cord. In the latter the degeneration consequent upon a lesion on one side of the brain, occupies two definite situations in a transverse section of the cord; the larger tract of degeneration (crossed pyramidal tract) occupies the lateral column of the side opposite to that of

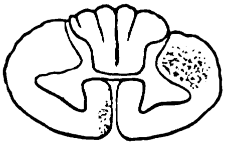


FIG. 263.—DEGENERATION OF THE SPINAL CORD.

Secondary to a lesion of the right hemisphere; *right* direct pyramidal tract, *left* crossed pyramidal tract (Mott). (See also fig. 264.)

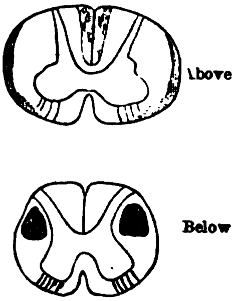


FIG. 264.—TRACTS OF DEGENERATION ABOVE AND BELOW A TRANSVERSE DIVISION OF THE CORD.

the cerebral lesion, the smaller tract (direct pyramidal tract) occupies the anterior column of the same side as that of the lesion. The fibres composing this smaller tract are believed to cross the middle line along the whole length of the cord to be distributed to the opposite side of the body. This coincides with the results of the experiments given above, to the effect that motor channels cross in major part at the decussation of the pyramids, in minor part throughout the spinal cord. The degenerated tracts taper downwards in both cases, the crossed tract being traceable further down the cord than the direct tract; the degeneration does not extend to the anterior roots, *i.e.* it is limited by the cells of the anterior cornua.

Ascending degeneration after hemisection of the cord, *e.g.* in the dorsal region, takes place on the same side as the injury in the postero-median column up to the nucleus of the funiculus gracilis, and in the direct cerebellar tract. It may also occur in consequence of destruction of spinal ganglia, or of division of roots between ganglia and cord; in this case the degeneration is limited to the posterior columns and absent from the cerebellar tracts—facts which are taken to signify that ascending fibres of the cerebellar tract are connected with cells in the cord below (cells of Clarke's column), while fibres of the posterior column are in uninterrupted continuity with posterior root-fibres and ganglia. These fibres do not, however, pursue an unbroken course to the cortex; the degenerated tract ends at the medulla, and must therefore form connection with cells in this situation (postero-pyramidal or gracilis nucleus). The cerebellar tract on the other hand is traceable through the restiform body into the cerebellum.

The above described are the main tracts along which systematic degenerations have been followed down and up the cord; we may however add, without entering upon comment or discussion, (1) that 'ascending' fibres, in more or less abundance, have been found degenerated in other situations—in the antero-lateral and in the posterior columns; (2) that a small patch of fibres in the posterior column (referred to by pathologists under the name of 'comma tract') undergoes descending degeneration after section of the posterior roots; (3) that ascending and descending degenerations taken together do not include the entire area of the white columns, but leave a considerable remainder, especially in the immediate vicinity of the grey matter, the fibres of which suffer no degeneration, and are therefore considered to be commissural between cells at different levels.

It should moreover be expressly stated that tracts of degeneration do not constitute direct evidence that such tracts are normally functional channels in the direction of degeneration. They indicate lines of trophic influence derived from 'centres' which have been destroyed, or from which the fibres have been separated. It is, however, considered probable that such lines of trophic influence coincide with lines of functional impulses—but we must recognise that the inference is not unimpeachable—as a matter of fact we know that afferent nerves of the posterior root divided beyond the ganglion undergo 'descending' degeneration. The terms are also open to the objection that, as in the case of nerves, the degeneration does not gradually ascend or descend, but that it simultaneously invades the entire length of a tract separated from its trophic centre.

(3) **Development.**—The various white tracts of the spinal cord are not developed simultaneously, but successively, the fibres composing them acquire their medullary sheaths at different dates, so that in embryos at various stages, various tracts may be distinguished and separately followed. As regards this order we may, without going into details, quote the main conclusions of Flechsig's investigations; the first apparent fibres are the peripheral or root-fibres connecting the spinal grey matter with the periphery—sensory, then motor; the next are the commissural fibres connecting grey matter at different levels; next the centripetal tracts from cord to bulb and cerebellum; finally the centrifugal tracts from cerebrum to cord. The most important point which has been thus brought out is that the pyramidal tracts above described as degenerating in consequence of cerebral lesion are the last comers, and that they appear simultaneously with the cortex cerebri from which they take their origin. This is corroborative evidence of the view that the pyramidal tracts are motor channels from the cortex. On man this motor or pyramidal system does not appear until birth or a few weeks later, before which it is not possible to distinguish a pyramidal tract by means of either of the methods by which tracts of medullated fibres are best demonstrated (Weigert's or Pal's method); these tracts are not well developed until the end of the first year, and even then are recognisable as the youngest of the spinal tracts, being composed of fine fibres (2 μ); whereas in the adult state

they are second only to the direct cerebellar tracts as regards the diameter of the majority of their fibres (5 to 10 to 15 μ). In the development of the pyramidal tract two further points are distinctly noteworthy. Firstly, the fact that its nerve-fibres go through three recognisable stages:—appearing as naked axis-cylinders (fifth month), as fine medullated fibres (ninth month), finally as coarse medullated fibres. Secondly, the probability, almost amounting to certainty, that the pyramidal tract, appearing as the last comer in the cerebro-spinal axis, develops in a centrifugal manner, pushing and insinuating itself along the lines which it finally occupies. A third point should also be alluded to, viz. that the relative proportion between direct and crossed tracts is liable to vary; ordinarily the direct is to the crossed as 1 is to 9, but the proportion may be occasionally 1 to 4 or 1 to 1, and very exceptionally the entire pyramidal mass may fail to cross, being continued as an abnormally large anterior column.

To sum up the considerations contained in the foregoing pages—experiment, clinical observation, the study of development and of degeneration concur to testify that in man the *motor* channels from one side of the brain pass to the opposite side of the body *viâ* the lateral column of the opposite side, and the anterior column of the same side; the former channel, called the crossed pyramidal tract, is the larger, and crosses the middle line in the bulb; the latter channel, the direct pyramidal tract, is the smaller, and crosses the middle line in the spinal cord. As regards *sensory* channels it is proved that these cross from one side of the body to the opposite side of the brain, but as to the precise locality of the crossing, evidence is conflicting. According to the older experiments, the chief crossing is in the cord; according to newer experiments, and to the collateral but not perfectly conclusive evidence of development and of ascending degeneration, the chief crossing is in the bulb, above the decussation of the pyramids.

The spinal cord as a centre of reflex action.—We have seen that the grey matter of the spinal cord constitutes a series of centres, and that the movements over which they preside are pre-eminently of a *reflex* character. Certain movements, however, of undoubted spinal mechanism stand out from this category, and are more commonly characterised as *automatic*; certain other movements, also of undoubted spinal mechanism, demonstrable only on the lower vertebrates, are manifestly appropriate to definite ends, and have the appearance of being volitional in character to such a degree that the expression *psychical* has even been used to characterise them. Yet these movements in no wise detract from the statement that the spinal cord is the typical centre of reflex actions in their purest form, namely, immediate, unchosen, fatal responses to peripheral excitations, without the intervention of consciousness and volition. The aimless movements of the limbs of the paraplegic patient are a glaring instance of this kind of action in its lowest form. A grade higher, and the reflex act is something more than an aimless spasm; it is a defensive act with animal self-preservation as its result, a character which may very generally be detected in spinal reflex acts. A grade higher still, and the spinal reflex act is so frequent and habitual as to *appear* to have become independent of peripheral excitations, and now it receives the name of an automatic action. Such actions are very evidently defensive and self-preservative as regards animal life. No sharp boundary line can be drawn between the reflex and the automatic; as we have seen in Chapter viii., the two expressions overlap, and are often used indifferently; but, contrasting extreme cases of each, we may say that the reflex act is occasional and its excitation definite, while the automatic act is habitual and its excitation indefinite. We may also repeat here a consideration to which allusion has already been made (p. 299), viz. that spinal action is relatively best developed in the lowest vertebrates; in the highest vertebrates the cord is a comparatively degraded centre.

Further analysis of the mode of action of the spinal cord as a centre can be best made on decapitated frogs. The following are the chief experiments and observations which may be repeated.

1. *Summation of stimuli.*—A series of comparatively weak stimuli is far more effectual in eliciting a spinal reflex action than a single stimulus of much greater strength. This may be demonstrated by applying induction shocks to the skin, or, better (in order to eliminate the possibility of the summation having its seat in the cutaneous nerve-endings), to the central end of a divided sciatic nerve. Very weak tetanisation is effectual, while much stronger single shocks give no effect at all; but even single shocks will become efficacious above a certain limit of strength. To use an analogy—a nail is driven home better by a series of comparatively light blows than by one single heavy blow.

2. *Diffusion of stimuli.*—If the skin of one limb be stimulated by induction shocks of minimal strength, the first muscular reaction occurs in that limb. If the strength of stimulation be increased, the opposite limb of the same segment also contracts; on further increased strength of stimulation, the other limbs enter into action. Thus if the skin of the right inferior extremity be stimulated the muscular responses occur: (1) In the right inferior extremity. (2) In the right and in the left inferior extremities. (3) In the inferior and in the superior extremities. That is to say, excitation diffuses in the grey matter of the spinal cord, first transversely, then longitudinally.

3. *Inhibition of stimuli.*—Two successive stimuli on the same spot summate. Two successive stimuli on different spots may either summate or interfere with each other. Two simultaneous stimuli on different spots more commonly interfere with each other. These statements are not to be taken as absolute, but only as expressing a general rule to which there are many exceptions. The best experiment to demonstrate inhibition of stimuli in the spinal cord is made on the decapitated and brainless frog by means of chemical stimulation. The tip of one toe is stimulated by being dipped into weak acid (H_2SO_4, 2 per 1,000), and the interval between application of stimulus and retraction of the limb is measured. A crystal of common salt is applied to the upper part of the cord and the experiment is repeated; the reaction interval is prolonged, or it may be necessary to use strong acid to get any reaction at all. This mode of testing the excitability of the cord by stimulating the skin with weak acid is known as Türck's method; the experiment above described with salt is a modification of one by Setschenow, in which it is applied to the optic lobes in order to demonstrate their inhibitory action on the cord.

4. *Time of reflex action.*—Türck's method has been employed to determine the interval between stimulus and reaction, but is open to the objections that it necessarily includes the time during which the acid is soaking through the skin, and that the stimulus is in reality an increasing one, the exact moment of explosion of which it is impossible to determine. The real time of reflex action is best found by applying single induction shocks to the central end of a divided sciatic, and correcting the total time of reaction by the amount lost in transmission along nerves and in delay at the muscle. Measured thus, the true reflex

time, *i.e.* that occupied by the elaboration of a stimulus in the spinal cord, is found to be only ·01 to ·015 second; whereas by Türck's method the interval between dipping and contraction may be anything between 5 and 30 seconds.

On mammalia the true reflex time of the spinal cord has been imperfectly studied. On an intact animal we cannot be certain that a movement, which is to all appearance reflex, is in reality effected through the spinal cord alone; it may be a reaction from the brain. This especially applies to man: the prick of a needle will cause a so-called reflex withdrawal of the hand, and the total interval between the two events will be above $\frac{1}{10}$ second; but it is probable that this is a cerebral reaction involving sensation (see p. 534). Winking of the eyes in response to a stimulus applied to the conjunctiva is probably the nearest approach to a true reflex act demonstrable on man; the organ of return of action being in this case the spinal bulb, and the total interval between stimulation and response $\frac{1}{20}$ second. This is the shortest known reflex time on man, and it is noteworthy that stimulation of one eye causes simultaneous reaction of both eyelids, there being no time lost across the middle line. We shall see that on the frog it may be shown that a crossed reflex suffers more delay in the cord than an uncrossed reflex. To determine the spinal delay on mammalia it would be necessary to measure the undoubtedly spinal reflex of animals after division of the cord, or that of a paraplegic patient. The latter observation has not been made; with regard to the former, Franc and Pitres give in the case of the dog ·022 to ·040 second for a reflex on the same side, ·048 to ·058 for a reflex on the opposite side.

Adaptive or 'psychical' reactions.—To what degree a brainless frog is superior to a brainless dog or man, may best be realised by the following experiment on decapitated frogs. The frog is suspended, the side of its body is touched with strong acid; it raises the leg of the same side, and makes wiping movements at the spot of irritation; the leg of that side is held or removed, the animal may then curl the other leg round and wipe the spot of irritation. From these, among other observations, Pflüger was led to apply the term psychical to the spinal function of the frog; and although the term may appear somewhat extravagant, it serves to call attention to the extremely complicated, and, to all appearance, discriminative and appropriately adapted reactions of the spinal centres in animals.

Action of strychnia.—Strychnia causes g the excitability of the spinal cord of all ver dog, a rabbit, or a frog, having received a strychnia, dies in tetanus with the limbs e: muscles of the body firmly contracted. mammalian animal, the tetanus involves ε ments of respiration and circulation, and de rigid state of the muscles passing off in a fe the grey matter of the cord quickly ceases to a frog, even after a considerable dose, the ani hours, but is not in reality dead; cutaneou cient, circulation continues, and the spinal That the contracted condition of the muscl the spinal cord, may be proved at once by when the tetanus gives way and the anin That the exaggerated action does not in any increased excitability of either nerve or m tained by testing them with induction shoc advisable to protect one limb by ligature and compare its nerve and muscle with those of the opposite unprotected limb, when it will be found that so far from being more excitable, the muscles of the unprotected limb are much less excitable than those of the protected limb; they exhibit, in fact, signs of having been fatigued by the excessive action into which they have been put by the spinal

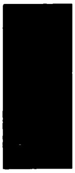


FIG. 255.— REDUCI EXCITA STRYCH

Another noteworthy feature in the strycl frog, is that the contraction is not (at any r intoxication) continuous and unbroken, bu muscular tetanus is incomplete, with a cc of 8 to 10 per second—indicating that the charging impulses at this rate.

Several further facts relating to the act the cord are studied on frogs. Summati single weak stimulus is as effectual as a seri sion of stimulation is excessive, the excitati ently in all directions in the grey matter, and cannot be shown to extend transversely and longitudinally in proportion to its strength; in short, we may use for a stimulus applied to the strychninised cord the same phrase as that by which we characterised a stimulus applied to a quiescent heart—'all or nothing,' the stimulation produces no effect or a complete one, consisting in a convulsion of all the muscles of the body.

It might be expected that with an exaggeration of excitability such as that just described, we should find the reflex time shortened. But the opposite is the case; although excitability is increased, the reflex time is prolonged, and this to such a degree that we can analyse the phenomenon on strychninised frogs far more minutely than is possible in a normal condition.

If on a slightly strychninised frog we measured the lost times: (1) of direct excitation, (2) of reflex reaction of the excited limb, (3) of reflex reaction of the opposite limb, (4) of reflex reaction of the limb above, we should find that (2) is about $\frac{1}{100}$ second longer than (1), that (3) and (4) are respectively about $\frac{1}{100}$ second longer than (2)—*i.e.* that the time lost in transverse and in longitudinal diffusion in the cord is about the same as that of a simple reflex process. In a more deeply intoxicated frog, notwithstanding the greater excitability, the lost time is much increased, that of the simple reflex sooner and to a much greater extent than that of the transverse or longitudinal diffusion; the simple reflex time may be increased tenfold while the diffusion time is only doubled.

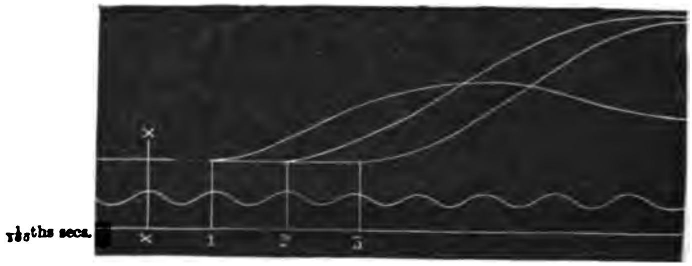


FIG. 256.—FROG.

Lost times of (1) a direct muscular contraction; (2) of a simple reflex contraction; (3) of a crossed reflex contraction: × marks the moment of excitation.

Centres of the spinal cord and bulb.—The actions ordinarily administered by the spinal cord are of various characters, and [illegible] credited with numerous centres 'for' various actions. In passing these in review it will be convenient at the same time to consider the central functions subserved by the spinal bulb, which likewise administers a variety of actions of a reflex or of an automatic character. The cord and bulb are in this connection to be regarded as of co-ordinate rank, constituting conjointly a medullary axis of grey matter—medulla oblongata and medulla spinalis—which acts as the intermediate between the brain and the periphery.

The spinal cord is credited with the following centres:

Movements of limbs	page	490
Musculo-tonic	„	491
Respiratory	„	145
Cardiac accelerator	„	105
Vaso-motor	„	109
Sudorific	„	247
Cilio-spinal	„	435
Genito-spinal	„	109
Ano-spinal	„	165
Vesico-spinal	„	244
Trophic	„	355

The spinal bulb is credited with:

Respiratory	expiratory inspiratory	page	145
Vaso-motor	constrictor dilatator	„	99, 109
Cardiac	accelerator inhibitory	„	98, 109
Centres of phonation and articulation; coughing and sneezing		„	149
Sucking			—
Mastication		„	159
Deglutition		„	160
Vomiting		„	166
Co-ordinating		„	491
Convulsor		„	491
Closure of eyes		„	486
Dilatation of pupil		„	435
Salivary		„	178
Sudorific		„	247
Diabetic		„	220

The expression 'centre *for*' such and such an action, is to be deprecated; it implies a mapping out of the bulb and cord into departments far more definite and artificial than the reality, and an illegitimate dictation of final causes. And this artificial scheme is pushed to the verge of absurdity when centres such as the 'convulsive' or 'vomiting' centre are invented, centres for sneezing, laughing, crying, sucking, coughing, &c. Such 'centres' as these do not deserve the name. Certain actions are carried on by groups of associated muscles served by nerves which spring from different parts of the bulb and cord; these different parts are anatomically centres, but it is an abuse of language to call them centres *for* such actions. There is no justification for speaking of a centre for muscular tone, and of a centre for movements of the limbs, as if they were separate real organs; cilio-spinal, genito-spinal, ano-spinal, vesico-spinal, convey a notion of definiteness far in excess of actual facts, which are simply to the effect that nerves to the iris, genitals, rectum, and bladder are connected with the spinal cord, and that certain reflex actions of these various parts require the integrity of the cord, and of the nerves which connect them with it. So again with regard to the so-called sudorific and trophic centres, and the somewhat less indefinite cardiac, respiratory and vaso-motor centres in the bulb and cord; these are one and all indefinite organs and not to be regarded in the light of anatomically definable nuclei of grey matter. Nerves which are channels of sudo-motor, vaso-motor, and respiratory acts are connected with the medullary axis at certain points; this is the simple anatomical fact, to a knowledge of which it is no addition, to say that they are the specific centres for certain functions. With such or some such reservations made, we may consider in detail the different kinds of actions which are controlled from the medullary axis.

Movements in general.—Simple reflex movements of the limbs may result from peripheral stimuli; complex, orderly, co-ordinated movements, such as those of locomotion, may also be performed automatically. Movements of both these kinds are governed by the spinal cord, and are presumably administered by it; it is only on the lower animals, however, that the experimental proof has been given of the performance of co-ordinated movements after the removal of the brain and bulb. Various notable experiments have been made on frogs and on snakes in this connection. A decapitated frog, possessing no nervous centre above the spinal cord, is a living machine which moves only when it is set in motion by a stimulus—when it does move, however, it exhibits indications of a high degree of complexity (p. 486). The headless frog makes definite and appropriate efforts to remove an irritant applied to its skin; if it fail with one leg, it makes attempts with the other. A decapitated snake likewise makes highly complex movements: twines round a stick, bends its body away from a hot poker. On the higher animals even, highly complex movements may still be performed; ducks and ostriches have been known to run about after decapitation. Mammalia, however, exhibit little beyond simple reflex movements, though even in their case the movements are such as to suggest self-defence.

There is no reason whatever for admitting the existence of any distinct *co-ordinating centre* in the bulb or cord. When the co-ordinate and measured movement of a group of muscles occurs, due order and measure of outgoing impulses are of primary necessity; a co-ordinate character is not imposed upon the action of some centres by other specially co-ordinating centres. There are no grounds for admitting co-ordination as a special function of special centres; nor is there any reason for admitting the existence of any distinct *convulsion centre* in the medulla or cord. When a convulsive action occurs outgoing impulses are without order and measure. An incoördinate and excessive character is not imposed upon the action of some centres by any other specially convulsive centre. There are no grounds for admitting convulsion as the special function of any special centre.

The *musculo-tonic* action exercised by the spinal cord keeps the whole muscular system in a state of slight contraction or tone. There is no reason for attributing such action to special centres, it is in any case not to be regarded as anything beyond a slight and continuous motor discharge, and there is no reason for regarding it as different in kind or origin from the stronger and discontinuous motor discharges which cause muscular contractions. The very existence of a musculo-tonic action has been questioned, but is nevertheless to be regarded as established by sufficiently conclusive experiments. Brondgeest's experiment to demonstrate muscular tonus, consisted in the simple suspension of a frog after section of one sciatic nerve; the normal limb remained flexed, the other limb hung loose. Cyon performed the experiment after section of the posterior roots of the spinal nerves which go to form the sciatic, with a similar result, and has shown that the tonic flexion ceases when the limb is deprived of its skin; these are proofs that muscular tone is a continuous reflex action caused by a continuous centripetal influence, seeing that it ceases if the afferent channels from the limb are interfered with.

The phenomenon of so called *tendon-reflex* on man bears a close relation to muscular tonus. It consists in the sudden contraction of a muscle when its tendon is smartly struck, and is best known in the case of the rectus femoris when the ligamentum patellæ is struck. It is not a reflex contraction, for its latent period is about the same as that of muscular contraction caused by direct electrical stimulation, *i.e.* much too short to be acceptable as the time of a reflex contraction; but its indispensable condition is the reflex muscular tonus above spoken of; for if the nerves supplying the muscle be cut, or if only their motor roots be cut, or if only their sensory roots be cut, the reaction is abolished, *i.e.* the integrity of the reflex arc is a necessary condition of the reaction. It has great value as a clinical test, especially in the diagnosis of locomotor ataxy; its abolition is an early and very characteristic sign of the onset of the disease. The opposite change, viz. an exaggeration of the reaction, usually occurs as a sign of descending degeneration of the cord in consequence of lesions of the cord or brain, and the exaggeration is generally accompanied, or very shortly followed, by a state of permanently increased muscular tonus—the '*contracture*' of clinical medicine. 'Contracture,' if not of very old standing, is cut short by section of the motor nerves, and disappears when death takes place.

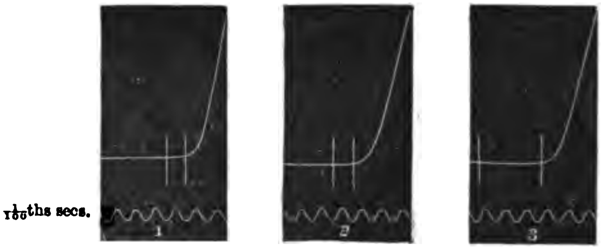


FIG. 257.—RABBIT.

Time measurements of (1) a direct contraction, (2) of the tendon phenomenon, (3) of a reflex contraction.

The tonic contraction of the sphincters of the rectum and bladder is probably of a similar nature, viz. a reflex spinal tonus; incontinence of fæces and of urine are among the symptoms of disease of the lumbar portion of the cord, and Heidenhain has shown experimentally on rabbits that the resistance of the vesical sphincter to intravesical pressure is greater during life than after death, thus proving that the c to elasticity, but to elasticity reinforced b

Respiratory centre.—The movements a very definite act carried out by musc nerves from a certain definite part of the influenced through afferent nerves, and b in a manner which has been definitely The term 'respiratory centre' has thus a than, for instance, such terms as 'conv miting' centre. It is anatomically that pa from which originate the phrenic and pneu situated at the lower part of the bulb and

Definite nuclei of grey matter have, experimentally isolated as a respiratory c struction of the lower part of the spinal instrument introduced between the occip sudden death by cessation of respiratory m applied to this part the sensational name o vital,' or 'respiratory centre,' have nov meaning, and signify a part of the bulb nected nerves whose integrity is necessa of respiratory movements, that is to say, life. The respiratory centre is situated in in lesser part in the upper part of the spi action may be characterised as reflex a inasmuch as it may be temporarily incre occasional centripetal impulses; automatic to go on of itself, being in reality kept going These continuous stimuli reach the respirat (1) the state of the blood—reduced blood i blood is depressant of its excitability; (nerves. But these matters have already the heading of respiration. As regards t of the spinal cord and bulb we have alre physiological facts in a previous section.

We may, indeed, bring our review o actions of the bulb and cord to a close; its sufficiently answered if the lists given on appended the references to each particular to bring home to the mind the number a functions to which the integrity of the me sary. It should also be realised that the closely congregated nuclei of grey matter (see figs. 259, 260) located in its upper or bulbar expansion, are concerned in the performance of those fundamental functions which are of most immediate importance to the living body—respiration, deglutition, regulation of the heart and of the vessels. And we may in this connection conclude with a reference to the group of cardinal symptoms which are characteristic of bulbar paralysis, *i.e.* of an impaired medulla oblongata; these are a progressive imperfection of articulation, of mastication, of deglutition, and of phonation—'glosso-labio-laryngeal-pharyngeal' palsy.

THE CRANIAL OR BULBAR NERVES.

It will be convenient at this stage to review the physiological anatomy and chief functions of the cranial, or so-called cerebral, nerves. These nerves, twelve on each side, emerge from the base of the brain at points indicated in fig. 258. From this their superficial origin their fibres are traceable to nuclei of grey matter, which are clustered together in the neighbourhood of the fourth ventricle as indicated in figs. 259 and 260. With one exception (namely, the first or olfactory) the cranial nerves are functionally connected with the cortex of the opposite side, and, as in the case of the spinal nerves, there are no direct fibres between cortex and the cranial periphery; every fibre has at least one spinal cell in its course. Thus in the case of cranial as in that of spinal nerves, the path between cortex and periphery is divisible into at least two stages: one between cortical and bulbar cell, and one between bulbar cell and end-organ (muscle or epithelium). Thus, properly speaking, all cerebral and spinal motor and sensory nerves (with the exception of the first and second) are cerebro-spinal as regards their course, the 'cerebral' nerves having their spinal relay in the bulb, the 'spinal' nerves having theirs in the cord, in either case across the middle line; and if a classification is to be made into groups, that which most commends itself is into *spinal* and *bulbar* groups, the latter comprising the first twelve nerves, exclusive of the first and second, which occupy an exceptional position, but inclusive of the third and fourth, which, although arising from nuclei imbedded in the mid-brain, are in line anatomically as well as functionally, with the sixth and twelfth nerves.

The cranial nerves are as follows:

	Name	Distribution
1.	Olfactory nerve	From nose
2.	Optic "	From eye
3.	Oculo-motor nerve	To eye muscles
4.	Trochlearis	To superior oblique
5.	Trigeminal	From face, mouth, nose. To muscles of jaw
6.	Abducens	To external rectus
7.	Facial	To facial muscles
8.	Auditory	From ear
9.	Glosso-pharyngeal	To pharynx. From tongue
10.	Pneumogastric	To and from heart, lungs, viscera
11.	Spinal accessory	To heart. To trapezius and sterno-mastoid. To larynx, pharynx, and œsophagus
12.	Hypoglossal	To tongue

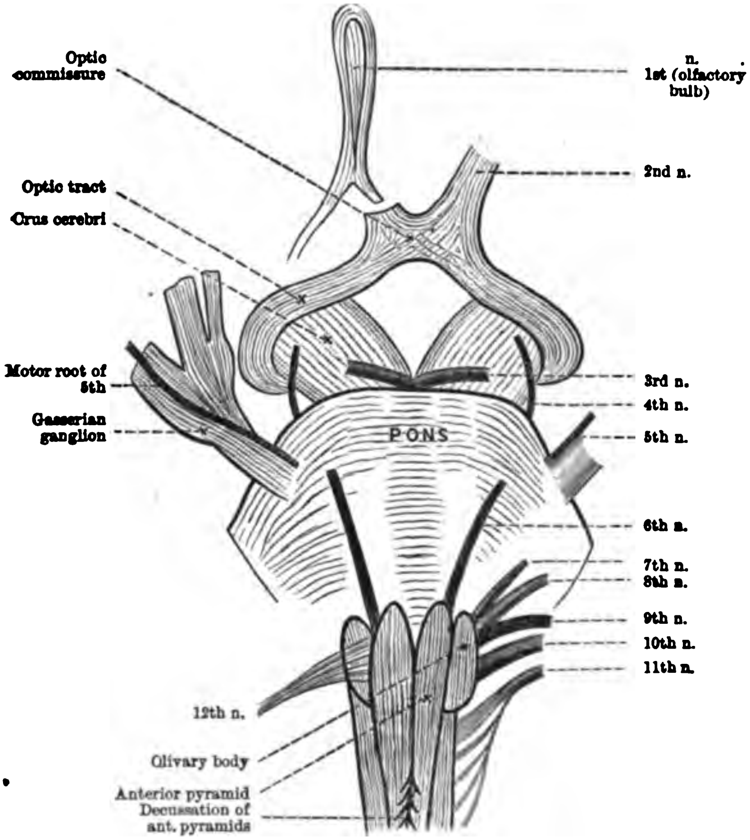


FIG. 258.—ANTERO-INFERIOR VIEW OF THE CRURA, PONS AND BULB (Diagrammatic) TO ILLUSTRATE THE SUPERFICIAL ORIGIN OF THE CRANIAL NERVES.

Traced back from their superficial to their deep origin, the cerebral nerves are for the most part (*i.e.* with the exception of the first four cerebral nerves) found to spring from nuclei of grey matter, closely congregated in the spinal bulb and pons beneath the floor of the fourth ventricle. The second, or *optic*, nerves by their optic tracts have extensive connections with the basal ganglia; fasciculi of the optic tract are traceable from three sources of origin—the lateral corpus geniculatum, the anterior corpus quadrigeminum, and the optic thalamus (posterior tubercle or pulvinar). The third, or *motor oculi*, and the fourth, or *trochlearis*, have their nuclei of origin in the corpora quadrigemina close to the sylvian aqueduct. The fifth, or *trigeminal*, has three distinct nuclei of origin; the median and smallest of these

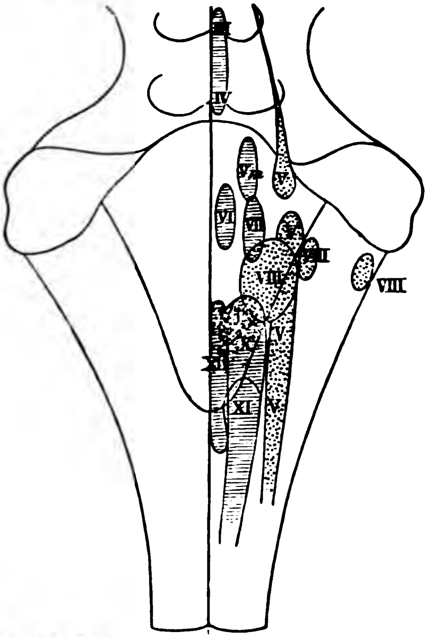


FIG. 259.—DIAGRAMS TO ILLUSTRATE THE POSITION OF THE BULBAR NUCLEI OF THE CRANIAL NERVES (After Erb).

Posterior aspect or 'floor' of the fourth ventricle exposed by removal of the pons and cerebellum and imagined as transparent. Motor nuclei indicated by horizontal lines, sensory nuclei by dots. Median group of motor nuclei III IV VI XII. Lateral group of motor nuclei Vm VII X XI. Sensory nuclei Vs VIII IX.

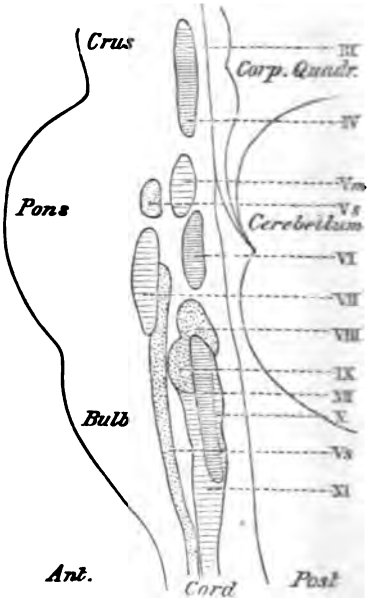


FIG. 260.—LATERAL VIEW OF THE RIGHT HALF OF THE BULB AND PONS EXPOSED BY A VERTICAL SECTION, AND IMAGINED AS TRANSPARENT.

In this view the lateral group of motor nuclei Vm VII X XI lie further from the surface of section and are indicated by lighter lines than the median group of motor nuclei III IV VI XII.

in the floor of the fourth ventricle is the 'motor nucleus,' the other two are the 'sensory nuclei,' and give origin to the 'ascending' and 'descending' roots of the nerve. The sixth, or *abducens*, has its nucleus of origin in the floor of the fourth ventricle. The nucleus of the seventh, or *facial*, lies deeper, below the floor of the fourth ventricle in the substance of the pons. The three *auditory* nuclei (eighth nerve)—median, lateral, and accessory portions—occupy a lateral situation in the upper part of the floor of the fourth ventricle; the more superficial or median or principal nucleus, and the smaller accessory part (which bears some resemblance to a spinal ganglion) give rise to the cochlear division; the lateral or deeper or superior portion gives rise to the vestibular nerve. The nerve of Wrisberg (pars intermedia of the seventh), from which the chorda tympani is formed, is also said to arise from the accessory nucleus. The ninth, tenth, and eleventh nerves—*glosso-pharyngeal, vagus, and accessory*—arise from an elongated nucleus of grey matter laterally situated in the lower part of the medulla and upper part of the spinal cord. The twelfth, or *hypoglossal* nerve, has its nucleus of origin superficially in the lower part of the bulb close to the middle line.

The *first, or so-called olfactory nerve*, is in reality a lobe of the brain; the true olfactory nerves are the eight or ten filaments which are connected with it. This lobe is the central organ of smell, the filaments are afferent of stimuli affecting the olfactory epithelium contained in the nasal mucous membrane. Unlike all other sensory impressions, it is supposed (but not known with certainty) that these do not cross the middle line, but that they have their central terminus on the same side of the brain.

The *second, or optic nerve*, is the continuation of the optic tract which is in connection with the corpora quadrigemina. The peripheral organ is a particular layer of the retina (rods and cones), and its cortical terminus is the occipital region. Section of the optic nerve causes blindness of the corresponding eye, excitation of its central end causes the sensation of light (subjective). It is an afferent nerve, conveying the stimuli of light which in consciousness give rise to the sensation of vision.

The fibres of the optic nerve cross the middle line at the optic chiasma; in the lower animals and in many mammalia (rat, guinea-pig, sheep, pig, horse, goat, deer) the decussation at the chiasma is complete; in other mammalia (rabbit, dog, cat, monkey, man) it is partial, each optic nerve giving a large proportion of fibres to the optic tract of the opposite side, and a small proportion of fibres to the optic tract of the same side; section or lesion of one optic tract in the case of man and of the higher mammalia causes paralysis of both retinæ (hemiopia) on the side of the lesion; antero-posterior division of the chiasma would presumably not cause total blindness; on other animals section of one optic tract would cause complete blindness of the opposite eye, and an antero-posterior section of the chiasma would cause total blindness. (See Figs. 219 and 277.)

The *third, or motor oculi*, supplies all the muscles of the eyeball (with the exception of the superior oblique and external rectus), the elevator muscle of the upper eyelid, the iris and the ciliary muscle. Section of the third nerve paralyses these, the eyeball is protruded and squints downwards and outwards, the upper eyelid drops, the pupil is enlarged, the eye cannot be accommodated. Excitation of its peripheral end reverses all these effects: the eyeball squints upwards and inwards, the upper eyelid is raised, the pupil contracts and there is spasm of accommodation. Both the above-mentioned groups of signs are of common clinical occurrence in consequence of paralysis or of irritation of the third nerve.

The fourth, or trochlearis, supplies the superior oblique muscle of the eyeball. Its section or paralysis causes the eye to squint inwards and upwards.

The fifth, or trigeminal, is a mixed nerve composed of a larger sensory portion and of a smaller motor portion; the former is a sensory nerve of the face, of the conjunctiva, of the teeth, of the mucous membrane of the nose, mouth and tongue; the latter is the motor nerve of the muscles of mastication, of the tensor veli palati and of the tensor tympani muscles. Nerve-fibres having direct control over nutrition (trophic) are assumed to be present in the fifth nerve, but the existence of these trophic fibres has not been conclusively determined (p. 356). The chief consequences of section of the fifth are: (1) paralysis of common sensation in its area of distribution, accompanied with impairment of smell and of taste; (2) paralysis of the muscles of mastication; (3) disorders of nutrition, of which the most notable effect is inflammation of the cornea leading to ulceration, and ultimately to complete destruction of the eyeball. The branches of the fifth contain numerous vaso-motor fibres derived from the sympathetic. These are mainly vaso-dilatator in kind.

The sixth, or abducens, supplies the external rectus muscle of the eyeball. Its section or paralysis causes the eye to squint inwards.

The seventh, or facial, is the motor nerve of the muscles of the face, *i.e.* it is the nerve which governs facial expression. By virtue of its chorda tympani branch it is also the channel of secreto-motor and of vaso-dilatator impulses; these are, however, attributable to sympathetic fibres. The gustatory fibres of the chorda tympani are derived from the glosso-pharyngeal. If the seventh nerve of one side is paralysed (Bell's palsy), the face on that side is smooth and expressionless, the eyes cannot be closed, lip movements, such as whistling or the articulation of labial consonants, are interfered with, and masticated food tends to collect between the cheek and gum, owing to paralysis of the buccinator; in consequence of the unopposed action of the muscles of the opposite or sound side, the face is drawn towards that side, particularly when the patient is made to smile or laugh. Section of the facial in young animals interferes with the nutrition of the muscles and bones of that side.

The eighth, or auditory, is the nerve of hearing, and plays an important part in equilibration. The peripheral organ is the internal ear, the auditory portion proper being in connection with the cochlea, the equilibratory portion in connection with the semicircular canals. Section of the auditory nerve causes deafness, giddiness, and staggering gait. Excitation of its central end gives rise to the subjective sensation of sound. *Menière's disease*, of which the characteristic symptoms are giddiness and staggering gait, has been found to be associated with affections of the semicircular canals.

The ninth, or glosso-pharyngeal, is a mixed nerve; it is the sensory and gustatory nerve of the posterior third of the tongue and adjoining mucous membrane of the mouth and pharynx, and the motor nerve of the stylo-pharyngeus and of the middle constrictor of the pharynx. Excitation of the central end of the glosso-pharyngeal inhibits the act of deglutition, and may excite vomiting.

The tenth, vagus, or pneumogastric, is a mixed nerve, with which we must include the internal branch of the spinal accessory, or eleventh nerve. The pharyngeal branches forming the pharyngeal plexus are the motor nerves of the levator palati and of the three constrictors of the pharynx. The *superior laryngeal* branch is the sensory nerve of the mucous membrane of the larynx, and the motor nerve of one of the laryngeal muscles—the crico-thyroid. The *depressor nerve* from the heart may have its course in the vagus trunk or in its superior laryngeal branch. After section of both superior laryngeal nerves the mucous membrane of the larynx is insensible, food or saliva can pass through the larynx without exciting coughing, and subsequently cause inflammation of the lungs. Stimulation of the central end of the superior laryngeal excites coughing, arrests respiration, and excites deglutition; it usually causes a reflex rise of blood-pressure, but may (if it includes the depressor) cause a reverse effect. The *inferior laryngeal* branch is the chief motor nerve of the muscles of the larynx. The *cardiac branches* contain the inhibitory fibres to the heart, and the depressor fibres from the heart; they also contain accelerator fibres derived from the sympathetic. The *pulmonary branches*, forming the pulmonary plexus, contain sensory fibres from the bronchial mucous membrane, and motor fibres to bronchial muscle. They also contain fibres, the excitation of which causes acceleration of respiratory movements. The *œsophageal* branches forming the œsophageal plexus, the *gastric* branches forming the gastric plexus, and the *intestinal* branches, are motor and sensory.

As regards the functions of the two portions of the vagus, viz. vagus proper and accessory, the former is mainly an afferent nerve, formed by fibres from the gastro-intestinal tract, from the heart, lungs, and larynx; the latter is exclusively an efferent nerve, giving off motor fibres to the levator palati, larynx and œsophagus, inhibitory fibres to the heart, and in all probability (although these points are not definitely proved) motor fibres to the bronchial muscle, to the stomach, and to the intestines.

Experimentally, section of the vagus high up in the neck causes acceleration of the heart-beat, impediment to deglutition, paralysis of laryngeal muscles, and—at a later date—inflammation of the lungs. Excitation of the peripheral cut end causes arrest of the heart's action, contraction of the larynx and of the œsophagus, and—but not so evidently—contraction of the bronchi, of the stomach, and of the intestine. Excitation of the central end causes reflex acceleration of respiratory movements, reflex inhibition of the heart, and reflex fall of blood pressure.

The eleventh or spinal accessory nerve divides into two branches—the internal branch, just considered, which accompanies the vagus proper, and the external branch, which is the motor nerve of the sterno-mastoid and trapezius muscles.

The twelfth, or hypoglossal, is the motor nerve of the lingual muscles, and of the genio-hyoid and thyro-hyoid muscles. Paralysis of the hypoglossal interferes with the movements of the tongue, which, when protruded, deviates towards the paralysed side.

The **sympathetic** system of nerves has already been frequently referred to; it is a main channel of vascular and visceral nerve control, and from a physiological standpoint its anatomy has been sufficiently described under the heading of vaso-motor nerves (p. 99). We allude to it in this place as being a system of nerve-fibres originating from the medullary axis formed by the grey matter of the spinal bulb and cord; the question formerly debated whether the sympathetic system is the independent companion of the cerebro-spinal system, or whether it is a dependent province of that system, may at the present day be regarded as finally answered in the sense of the second alternative. The clearest and most definite proof that sympathetic nerves are under spinal control is afforded (1) by the discovery that irido-motor fibres take origin from the spinal cord and bulb, (2) that vaso-motor fibres have a similar origin. Confirmatory evidence is derivable from the facts (3) that the fine medullated fibres, which there are reasons for considering to be vaso-motor, are traceable from the spinal cord into sympathetic nerves; and (4) that no reflex functions can be attributed to any sympathetic ganglion. As pointing in the same direction, although the fact itself is not uncontested, nor in any case demonstrative whether or not the sympathetic exercises independent function in the adult state, w may allude to its embryonic origin as an outgrowth from the medullary axis (p. 564). The old view, according to which the sympathetic system of vertebrata was regarded as homologous with the entire nervous system of invertebrata, is entirely abandoned; the homology is between the entire nervous systems of the two sub-kingdoms respectively.

CHAPTER XV

THE BRAIN

PAGE
502 General plan of its structure.
The hemispheres.
Cortex cerebri—Corona radiata—Internal capsule—Crura cerebri—Corpus callosum—The pyramidal or motor tract—The basal ganglia—Corpus striatum—Optic thalamus—The cerebellum—Corpora geniculata—Corpora quadrigemina.
506 Relation of cerebral development to intelligence.
508 Functions of basal ganglia—Of the cerebellum; forced movements.
510 The cortex of the brain.
512 Arteries of the brain—The Sylvian artery—The lenticulo-striate artery.
514 **The functions of the Brain.**
Hemiplegia—Crossed paralysis—Associated bilateral muscles—'Yoked' muscles and conjugate movements.
518 **Cortical localisation of function.**
519 Experimental excitability of the cortex cerebri—Motor area—The visual area—Their subdivisions.
527 Epilepsy—Epileptic foci.
529 Aphasia—Motor aphasia—Sensory aphasia—Word-blindness—Word-deafness—Recovery from aphasia—Deaf-mutes.
534 **The personal equation or reaction time.**
536 **Ratio between stimulus and sensation**—Weber-Fechner law.
539 **Sensory judgments—Contrast theories.**—Helmholtz, Hering.
550 **Fatigue—Sleep—Hypnosis.**

General plan of its structure.—Without entering upon any detailed description of the brain as given in anatomical text-books, we shall in this place consider and insist upon such points only as have immediate bearings upon the knowledge of its functions.

The cranium contains the two cerebral hemispheres and their basal ganglia (corpora striata, corpora quadrigemina, optic thalami), the cerebellum and the medulla oblongata. From the point of view of physiological anatomy we regard the medulla oblongata (=spinal bulb) as being spinal rather than cerebral; and we consider by itself the cerebellum, which, whatever its function may be, is not known to possess any action which it is customary to call 'cerebral.' As regards the basal ganglia, our attention becomes directed to them less on account of any definite functions which have been assigned to them, than because they occupy the isthmus of the brain and are thus on or close to the path between brain and body. Our physiological study of the brain is thus simplified, and comes to be directed almost exclusively to the surface of the hemispheres, and to the tracts which connect them with each other and with the nerve channels which emerge from the base of the brain: these are the *crura cerebri* and the *cranial nerves*. Viewed broadly, the brain is a mass of white matter with nuclei of grey matter deeply embedded in it, and with a sheet of grey matter about 2 millimetres in thickness covering the folds, fissures, and convolutions of its surface. This superficial grey matter, or *cortex*, is the brain proper, the organ of sensation, judgment, and will; the white matter beneath leads into it sensory impulses, leads off from it

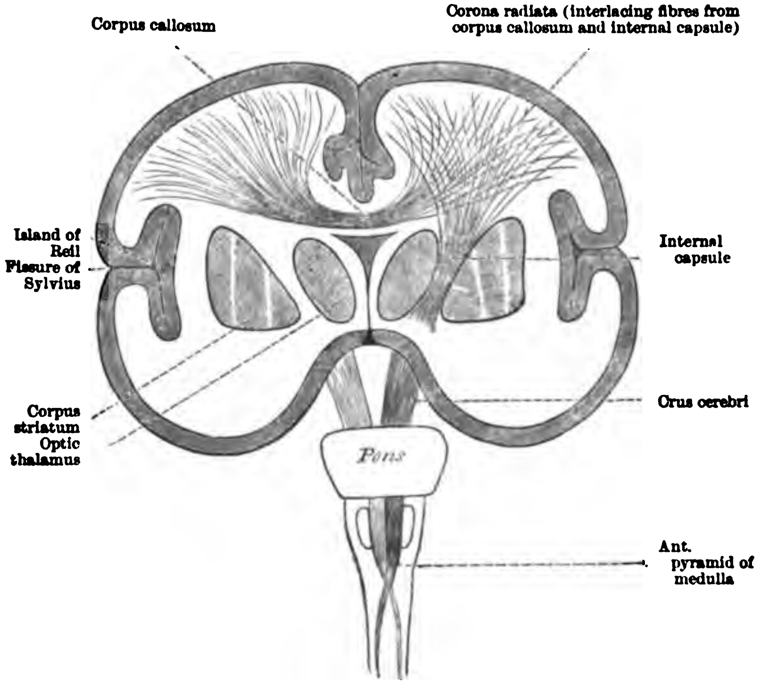


FIG. 261.—IDEAL VERTICAL SECTION THROUGH THE CEREBRO-SPINAL AXIS.

To illustrate the course of the pyramidal tract and its interlacement in the corona radiata with the commissural fibres of the corpus callosum.

motor impulses, and is simply a conducting mass composed of bundles of medullated nerve-fibres, disposed in a fan-like manner between the isthmus of the brain and the grey matter of the cortex, while below the isthmus it is continued as the white columns of the bulb and cord. This mass of white matter is known as the *corona radiata*; at the base of the brain, between the corpus striatum and optic thalamus, it forms a conical sheet of white matter known as the *internal capsule*, and proved to constitute the main channel of motion and of sensation. This main channel is continued as the two *crura cerebri*, which traverse the pons varolii, and are continuous with the white columns of the bulb and cord. It is probable that this main stream gives and takes fibres to and from the ganglionic masses which it skirts or traverses at the base of the brain, but to what extent we cannot say, and it is important to realise that a large portion

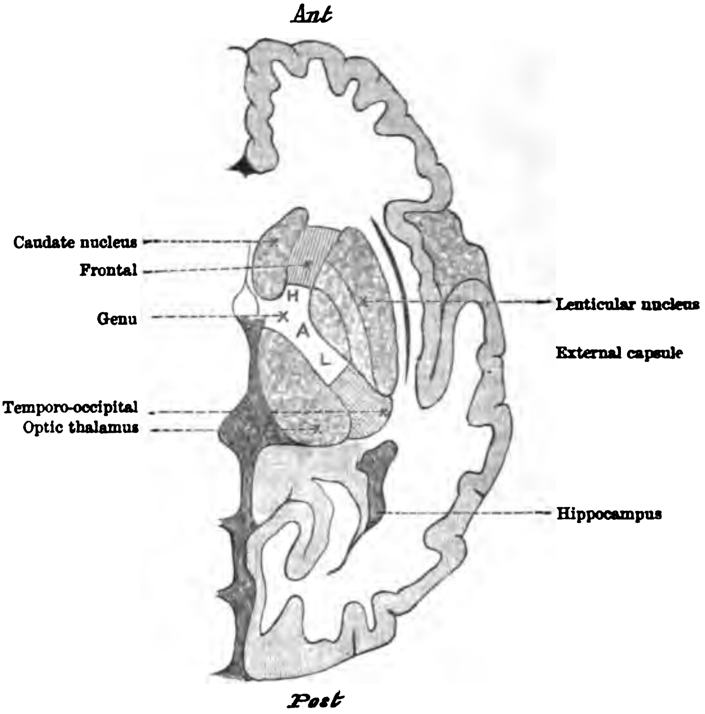


FIG. 262.—IDEAL HORIZONTAL SECTION THROUGH THE RIGHT HEMISPHERE AND BASAL GANGLIA.

To illustrate the position of the internal capsule taken in transverse section; H A L indicate the situations in the internal capsule of fibres governing the movements of the head, arm, and leg respectively. (After Charcot.)

passes directly through as a system of afferent and efferent channels between grey matter of cortex and grey matter of cord. The clearest testimony of this is afforded by the tract of descending degeneration which has been traced from cortex through corona radiata, internal capsule, crus cerebri, pons, anterior pyramids of bulb to the lateral column of the opposite side (the crossed pyramidal tract) and to the anterior column of the same side (the direct pyramidal tract.)

As regards localisation of motor and of sensory paths in the internal capsule and in the crus, pathological observations go to show that the posterior division of the internal capsule and the anterior or ventral portion of the crus (pes, crusta, or basis) are the main channels of motor and sensory impulses. It has further been observed that injury of the anterior two-thirds of the posterior division of the internal capsule is associated with hemiplegia; injury of the posterior third and of the temporo-occipital radiation, with hemianæsthesia; injury of the whole, with hemiplegia. *cum* hemianæsthesia. Descending degeneration from the frontal and occipital regions of the cortex, are respectively anterior and posterior to the pyramidal area in the capsule and crus, but are not traceable beyond the pons; whereas the pyramidal degeneration from the Rolandic region extends down the spinal cord (p. 480).

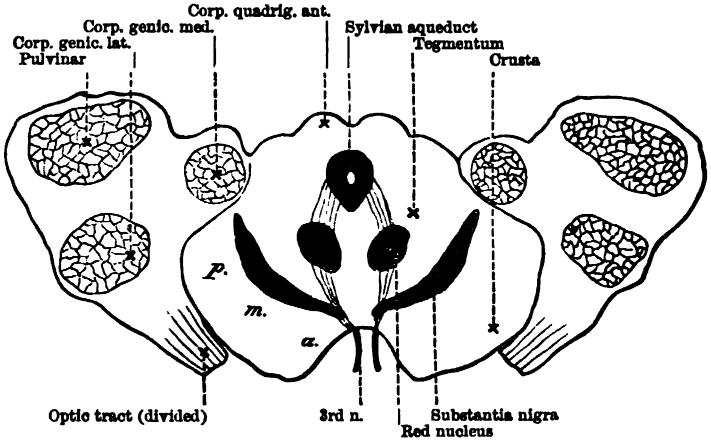


FIG. 263.—DIAGRAMMATIC TRANSVERSE SECTION THROUGH THE CRUS CEREBRI AND ANTERIOR CORPORA QUADRIGEMINA.

The letters *a m p* on the pes or crusta signify portions occupied by fibres from the anterior, middle or rolandic, and posterior regions of the cortex. (After Obersteiner.)

In addition to (1) the vertical system of fibres above described, the corona radiata contains (2) a horizontal system of fibres between the two hemispheres, having their chief path through the *corpus callosum*, and (3) numerous but scattered association fibres between the various convolutions. These last-named fibres are difficult to trace, least so perhaps in the gyrus fornicatus, in which there is a well-marked longitudinal system known as the cingulum. The vertical and horizontal fibres derived respectively from the internal capsule and the corpus callosum are also difficult to dissociate, being closely interwoven in their expansion through the corona radiata.

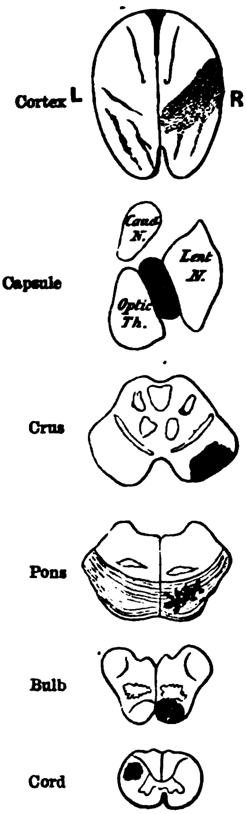


FIG. 264.—TO ILLUSTRATE THE PYRAMIDAL TRACT. (After Gowers.)

Relation of cerebral development to intelligence.—The brain, or, more precisely speaking, the cortex of the brain, is the organ of intelligent sensation and motion. Taken in the rough, the intellectual rank of animals bears some relation to the weight of the brain. Thus the average ratio between brain-weight and body-weight is in round numbers—

In fishes	1 to 5,000
„ reptiles	1 to 1,500
„ birds	1 to 220
„ mammals	1 to 180
„ ourang.	1 to 120
„ man	1 to 50

But mere weight of brain is not a regular index of degree of intelligence in individual cases; there are many exceptions to the general rule.

As regards man very similar considerations hold good—viz. taken in the rough the brain-weight of distinguished men is above, while that of idiots is below the average, and the brain weight of civilised men is above that of savages. Yet there are many individual exceptions to the general rule. The average brain-weight is—

Of Europeans	49 oz. or 1,390 grammes
„ Negroes	44 oz. or 1,250 grammes

As regards sex, the brain-weight cannot be appealed to in evidence of superiority on either side. The average male European brain weighs 49 oz.; the average female European brain weighs 44 oz.; but the average body-weights in the two sexes differ in about the same proportion. There is a more precise relation, though by no means an absolute one, between quality of brain and intelligence. The brain of an animal high in the scale is more complex than that of an animal low in the scale; in the ascending scale the hemispheres are relatively more developed both as regards size and as regards the complication of their gyri. In man the hemispheres have their maximum development; they cover all the rest of the cranial contents; their surface convolutions are of almost bewildering complexity. And now, taking a series of human brains, and comparing the convolutions of uncivilised and of civilised men, of men distinguished by abilities much above or much below the average, a general relation is traceable between complexity of surface and degree of intelligence. The basal ganglia are identical in the two cases, but the higher brain is more richly convoluted, its sulci are more numerous; the lower brain is simpler, its sulci are less numerous; the latter is practically a simplified diagram of the former; the effect of the difference is that the total area of grey matter is greater in the more highly than in the less highly organised brain. This is all we know with regard to the relation between quality of organ and quality of function; finer and more impalpable relations doubtless exist, but have not been demonstrated; the very absence of anatomical difference in the brains of average and of exceptionally able men leaves us, however, free to think, and justified in believing, that beyond quantity of grey matter there are differences in its quality. Perhaps its cells are more numerous, perhaps these more numerous cells are of better quality in the brains of the exceptionally able; but no microscopical or chemical proof has been given for or against such suppositions, still less is there any physical evidence available to distinguish the brain matter of 'good' men from that of 'bad' men.

Before entering upon the detailed consideration of the cortex cerebri we may pass in review such knowledge as we possess regarding the basal ganglia and the cerebellum. The term basal ganglia includes the corpora striata and the optic thalami, and may be taken to embrace the less prominent ganglionic eminences known as the corpora quadrigemina and the corpora geniculata.

The basal ganglia. The cerebellum.—Our definite physiological knowledge concerning the part played by the chief basal ganglia (*optic thalamus, corpus striatum*) is practically a blank. They form prominent and imposing masses of grey matter at the isthmus of the brain, but what part they may play in the elaboration of nerve impulses we do not know. From their anatomical situation they were formerly characterised as 'ganglia of interruption,' on the motor and on the sensory tracts respectively, but this conjecture is more and more weakened by additional pathological information. We know as positive that the motor tract merely skirts the ganglionic matter of the corpus striatum, without forming connections with its cells; we are more and more excluded from any right to suppose that the optic thalamus is a relay on the sensory tract. Our positive knowledge concerning the relation of the thalamus is limited to the degeneration, or rather deficient generation, which it suffers when the cortex cerebri is destroyed (v. Gudden).

It is a possibility that the internal corpus geniculatum and posterior corpus quadrigeminum may be the sub-cortical station of auditory sensation, but we have no positive assurance on the subject beyond the fact that these parts are in anatomical connection with the auditory nerve (cochlear division) of the opposite side.

The external geniculate and the anterior quadrigeminal bodies and the optic thalami (pulvinaria) are connected with the optic nerve.

The amygdaloid nucleus is connected with the olfactory bulb.

With regard to the part played by the cerebellum, our position from a physiological point of view is little better. A bulky organ cannot but be of importance; anatomically the cerebellum presents features which seem to promise great functional significance; it is connected by definite tracts with the cerebral hemispheres and with the spinal cord, it exhibits on section a more definitely regular structure than any other part of the nervous system, and histologically the disposition and regularity of the large cells of Purkinje seem to say that they play a definite and easily discoverable part in the control of the body. Yet we have not during the last fifty years added anything to, but have made reservations to and actual subtractions from, the conclusion of

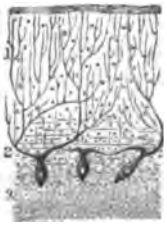


FIG. 265.—TRANSVERSE SECTION THROUGH THE CORTEX CEREBELLI × 50 diam. (Obersteiner.)

Flourens in 1831, that the property of the cerebellum consists in co-ordinating the movements incited from other nervous centres. Now, as then, the one definite function which we assign to the cerebellum is muscular co-ordination, the one prominent symptom of cerebellar disease is a staggering gait, and the only experimental effects of destruction or of excitation of different parts of the organ are forced movements; but these, as we shall see, are producible by lesions of many other parts of the brain. Clinically the cerebellum is supposed to play an important part in the government of the muscles and the maintenance of their 'tone'; but to the experimental physiologist it is an organ of disappointment. There is no paralysis after destruction of the whole cerebellum. There is no loss of intelligence. There is no evidence in favour of the conjecture that the cerebellum has anything to do with a genetic sense. The vertigo produced by electrical currents applied to the back of the head is probably not cerebellar, but due to excitation of the semicircular canals.

Lesions or excitation of the cerebellum to be of any effect must be unilateral, and the chief facts which have been observed are as follows:—Unilateral injury causes movements of rotation of the body *towards* the side of injury (*i.e.* clock-wise if the injury is on the right), and inclination to fall to the opposite side. Unilateral excitation causes muscles to contract on the same side. Dissections and degenerations indicate that the cerebro-cerebellar connection is a crossed one.

Forced movements.—We may take this opportunity of giving a short account of forced movements. Their characteristic is an overmastering action of the muscles of one side, or of large groups of 'synergic'[1] muscles acting in locomotion, in consequence of which the body twists round its long axis, or progresses in a circle of small radius (circus movements); sometimes the excessive action is such as to cause an animal to precipitate itself straight forwards and to turn somersaults in its progress, sometimes the tendency is to recede. It is probable that the central condition is one of excitation rather than paralysis, for hemiplegia is not attended by forced movements. With regard to the possible seat of excitation, we may recognise (1) that it is not in the cortex, the excitation of which, as we shall see, gives rise to epileptic movements; (2) that it may be due to lesions of the cerebellum, of the pons, of the crus cerebri, or of the basal ganglia; (3) that it may originate from the semicircular canals.

---

[1] 'Synergic' muscles are such as act together in habitual movements effected by the associated action of several muscles.

We may in some degree realise the nature of a forced movement by applying a constant current through two electrodes fixed to the back of the head. The somewhat complex sensations produced during the passage of the current are attributable to excitation of the brain, cerebellum, and semicircular canals; the head and body feel as if bent towards the anode, and in spite of our voluntary resistance the inclination becomes irresistible; the body bends and falls to that side, and the accompanying sensation is that of being dragged down. We have experienced a forced movement, and although under these conditions we must be in doubt whether the effect is by an uncontrollable excitation of the cerebellum, or of the semicircular canals, we may, from observations on birds, see reason to prefer the view that the semicircular canals rather than the cerebellum are the effective agents. Ewald has shown on pigeons that such forced movements produced by galvanism on the intact bird, are no longer produced after destruction of the semicircular canals, and are but little interfered with by destruction of the cerebellum.

Vertigo, or giddiness, furnishes a good illustration of the character of forced movements: subjectively, *i.e.* as felt by the subject, the prominent symptoms are distorted and exaggerated sensations of external objects, and uncontrollable muscular inclinations; objectively, *i.e.* as seen by an observer, the prominent sign is staggering, *i.e.* unco-ordinate forced movements.

THE CORTEX OF THE BRAIN

The cortex or grey mantle of the brain is divisible into the following regions: frontal, parietal, occipital, temporal,[1] mesial, and insular. The frontal region comprises the superior, middle, and inferior frontal convolutions, and the ascending frontal or præcentral convolution, which is situated in front of the fissure of Rolando or central sulcus. The parietal region comprises the superior and inferior parietal lobules, separated by the intraparietal fissure, and the ascending parietal or post-central convolution, situated behind the fissure of Rolando; in the inferior parietal lobule are to be recognised the supra-marginal gyrus at the posterior extremity of the Sylvian fissure, and the angular gyrus at the posterior extremity of the first temporal fissure. Three occipital convolutions are distinguished in the occipital region, and three temporal convolutions in the temporal region. The mesial aspect of the cortex, exposed by separation of the two hemispheres, includes the marginal convolution and gyrus fornicatus, separated by the calloso-marginal fissure and the hippocampal and uncinate gyri; the gyrus fornicatus is continuous with the gyrus hippocampi, forming with it the 'grand lobe limbique' of Broca, which should not be confused with 'Broca's convolution,' *i.e.* the third left frontal. The insular region or island of Reil is exposed by separating the lips of the Sylvian fissure; it is formed by a group of short convolutions occupying the lower surface of the frontal lobe.

---

[1] Or 'temporo-sphenoidal' of anatomists.

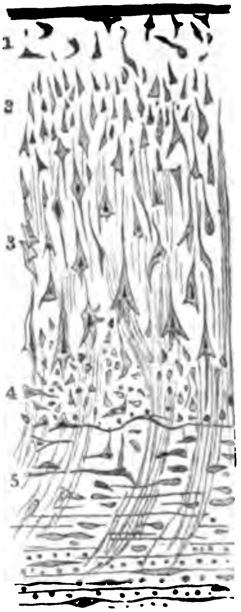


FIG. 266.—TRANSVERSE SECTION THROUGH THE CORTEX CEREBRI. FIVE-LAMINATED OR MOTOR TYPE. × 50 diam. (Meynert.)

Microscopically the grey matter forming the cortex of the brain consists of nerve-cells, nerve-fibres, and neuroglia, disposed in layers which are more or less distinguishable from each other. The stratification is best marked in the hippocampal region, which is characterised by a very regular layer of large nerve-cells; in other parts it is far less definite, so that it is almost impossible to identify each of the five layers of classical description (Meynert). A section of grey matter from a 'motor' convolution is, however, to some extent distinguishable by the prominence and number of large arrow-head cells (30 to 40 to 100 μ) in the deeper part of the so-called third layer; these are sometimes characterised as 'motor,' and are considered to be the analogues of motor cells in the anterior cornua of the cord and of Purkinje's cells in the cerebellar cortex. It no wise follows, however, because a nerve-cell is large, that therefore it is motor, and as regards the various cells above alluded to, those of the anterior cornua are the only ones whose claim to the term motor may be regarded as established upon sufficient data. The 'motor' cells of the cortex are so characterised because they are a prominent feature in the experimentally excitable area of the brain;

other large cells, whether in the hippocampus or in the cerebellum, are not qualified by any such designation. And, as a matter of fact, it happens that the large-cell layers are most definite in the very regions (hippocampus, cerebellum) the functions of which are most indefinite, and in all probability not motor. The supposition that the 'motor' cells of large muscles, or of 'large movements, or connected with long nerve-fibres, are 'large' as compared with 'motor' cells of small muscles, or of 'small movements,' or of short nerve-fibres, is a speculation as yet unsupported by any actual proof.

Arteries of the brain.—The arterial system of the brain is peculiar in two main particulars: (1) the large arteries by which it is supplied—two internal carotids and two vertebrals—form a free anastomosis at the base of the brain, known as the circle of Willis; (2) the branches which are given off from the circle of Willis, supplying the basal ganglia and the cortex, run their course to their several areæ of distribution with little or no anastomosis. It follows as a consequence of this disposition of the vessels that the circulation in the brain suffers little or no change by obstruction on the cardiac side of the circle of Willis, and that, on the

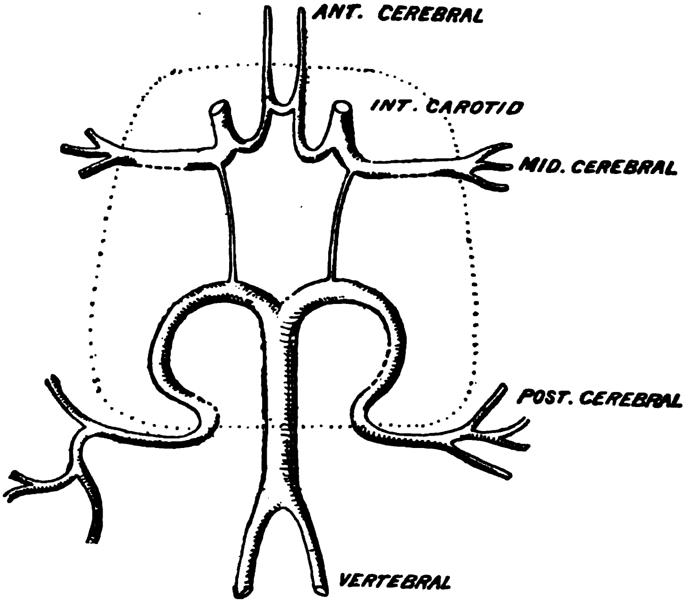


FIG. 267.—THE HEXAGON OF WILLIS. (After Charcot).

other hand, obstruction of a vessel beyond the circle of Willis causes damage which is confined to the area served by the obstructed vessel. The first statement is borne out by the experimental fact that, *e.g.* on dogs, it is not until all the four vessels leading to the circle of Willis are tied, that symptoms of arrested cerebral circulation appear. The second statement is most clearly exemplified by the well-characterised group of clinical symptoms which are caused when the left middle cerebral artery is blocked by an embolus. Considered from the point of view of its vascular supply, the cortex of the brain is divisible into three regions, supplied by the anterior, middle, and posterior cerebral arteries respectively. The cortical territory fed by the *middle cerebral* or *Sylvian artery*, which is the direct continuation of the internal carotid, is physiologically and pathologically the most important; it includes the convolutions in the vicinity of the fissure of Rolando, and those of the island of Reil, *i.e.* the so-called motor area and speech centre. If the Sylvian artery is blocked (and in the great majority of cases this happens on the left side) the consequences are motor paralysis of the right side and loss of speech, *i.e.* in clinical language right hemiplegia and motor aphasia.

In addition to the cortical system formed by branches of the three cerebral arteries, other branches from them are supplied to the basal ganglia, and form the ganglionic system of arteries. Those given off by the middle cerebral are of greatest pathological importance, as being the vessels most apt to give rise to hæmorrhage; one branch in particular, the *lenticulo-striate*, has been called the '*artery of cerebral hæmorrhage*' (Charcot), because it is most liable to give way; the hæmorrhage derived from it may compress or rupture the internal capsule, and so cause hemiplegia. As regards the ultimate distribution of the cerebral capillaries, the most noteworthy point is that the network is much closer and richer in grey matter than in white matter; the former is physiologically the more active, and requires to be more abundantly nourished with blood; a similar difference holds good in the case of the spinal cord, in well-injected sections of which, the closer vascular network of the grey matter defines the pattern of the cornua in the midst of the scantily supplied white matter.

It was formerly a debated question whether or no the amount of blood can vary within the cranium; taking into account that the cerebral ventricles are in communication with the subarachnoid space and filled with a serous fluid, there can be no doubt that more or less blood may enter the cranium expressing more or less serous fluid into the spinal canal. The subarachnoid and intra-ventricular fluid is indeed of great mechanical importance, forming as it does a bath within which the cerebro-spinal mass is protected from accidental shocks and sudden pressure.

The functions of the brain.—That the brain is the organ of intelligent sensation and motion is proved by the facts of comparative anatomy already alluded to, and by common experience. The same proposition is established by clinico-pathological facts, and by the study of animals after removal of a hemisphere or of the cortex. Experimentally we learn that after removal of the cortex an intelligent animal is reduced to the state of a non-intelligent automaton, responding indeed to stimuli, internal as well as external, but failing to interpret the significance of present events in accordance with bygone experience. A brainless dog is stupid; he may see a bone in front of his eyes without showing sign that he knows the meaning of a bone, or the use to which it may be put; he may hear the crack of a whip, but he no longer shows sign of fear, for he does not remember its sting; his former purposeful behaviour has entirely disappeared: in short, he has lost memory and judgment.

From clinico-pathological observations as well as from experiment we learn, moreover, that each hemisphere is the controlling organ of the opposite side of the body. Clinical cases of ordinary hemiplegia are every day found to be due to unilateral disease in the opposite hemisphere. Experimental extirpation or stimulation on one side of the brain is found to produce paralysis or muscular contractions of the opposite side of the body. These facts are, of course, referable to the crossing of motor and of sensory paths in the bulb and cord.

Typical common hemiplegia is limited to one side, but not infrequently cases of *crossed paralysis* occur, in which the arm and leg of one side and the face on the other side are paralysed, and it is found post-mortem that the combination is due to lesions on one side of the brain involving nerves or nerve-nuclei at the base of the brain, which are controlled from the cortex of the opposite side. A tumour in the vicinity of the pons, for instance, might interrupt the left pyramidal tract, and at the same time the left facial nerve or its bulbar nucleus; under these circumstances right hemiplegia of the limbs in combination with paralysis of the left side of the face would be produced, and the face would be drawn towards the paralysed side of the body, instead of from that side as in a case of common hemiplegia.

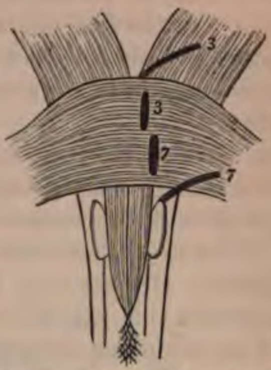


FIG. 268.—DIAGRAM OF THE CRURA PONS, AND BULB.

To illustrate the mechanism of crossed paralysis; the figures 3, 7 point to the nerves and nuclei commonly involved.

The fundamental notion that the muscles of one side of the body are connected with the opposite side of the brain requires to be supplemented by certain other considerations; it cannot be doubted that each side of the brain mainly governs muscles—or, more properly speaking, movements—of the opposite side of the body, especially in their unilateral and most highly specialised modes of action; but it is no less certain that from one side of the brain muscles of both sides of the body may be governed, this being especially the case in their bilateral and more automatic action. This principle is exemplified in the everyday clinical phenomena of hemiplegia; it is particularly striking in conjugate movements, as in the case of the head and eyes, and in bilaterally associated movements, as those of the respiratory and laryngeal muscles; it is also seen in the effect of experimental stimulation of one side of the cortex, a weak stimulus giving movement only on the opposite side, but a strong stimulus giving movement also on the same side of the body, though with less energy and with a greater lost time than on the opposite side.

In a typical case of hemiplegia all the muscles of one side of the body are not equally affected; the muscles of the extremities are most completely paralysed, those of the trunk not at all, or only partially on both sides. More generally expressed, the muscles which suffer most are muscles with unilateral action, engaged upon specialised movements, those which suffer least are muscles which are bilaterally associated in their actions. This bilateral association postulates communication across the middle line between symmetrical centres of the two sides of the body. The communication may be effected by commissural fibres between the cortical centres, or more probably by commissural fibres between bulbo-spinal nuclei. In unilateral convulsion (*e.g.* hemichorea) there is a similar but reversed inequality in the distribution of spasm on the two sides of the body; in the case of muscles of unilateral action, the convulsions may be limited to one side, but in that of muscles habitually associated in bilateral action, the convulsions always affect both sides. Moreover, it is possible that a muscle may be paralysed as regards its participation in a voluntary highly specialised manœuvre, while remaining efficient as regards its participation in reflex or in automatic action.

From all these facts two important consequences are to be drawn: (1) that each hemisphere, while mainly governing the opposite side, also takes part in the control of the same side, *i.e.* from any given cortical focus not only crossed fibres must exist, but also direct (or more probably *twice* crossed) fibres; (2) that particular movements rather than particular muscles are associated with cortical motor foci. The significance of this second statement will be better appreciated after the doctrine of localisation has been considered.

A remarkable feature in the history of a paralysis, especially one of cortical origin, is that the loss of motility gradually diminishes, as if the cortical blot were encroached upon from its periphery. A full discussion of the possible mechanism of the fading of a paralytic deficit would lead us too far; we must be content to say that even after making allowance for the progressive diminution of the collateral effects surrounding an acute lesion, it is necessary to admit that the recovery is in part due to the gradual assumption of control over paralysed parts by associated uninjured cortex; this assumption is particularly probable in the case of aphasia (p. 531).

Conjugate movements of the eyes, head, and neck.—We have learned in the section on vision that the movements of the two eyes are exactly equal and parallel for different directions of distant vision; both eyes are turned to the right or to the left, up or down, so that the object fixed gives images on corresponding parts of both retinæ. In movements directly upwards or downwards, muscles of the same name in each eye are associated in action; but in lateral movements the association is asymmetrical, *e.g.* the external rectus of one eye acts with the internal rectus of the other, and the peculiarity of this associated action seems still more striking when it is remembered that the external rectus is supplied by the sixth nerve, while the internal rectus is supplied by the third. A similar, if less striking, association of asymmetrical muscles on the two sides occurs in the rotation of the head and neck, which are turned to the right by the right inferior oblique and left sterno-mastoid muscles, to the left by the left inferior oblique and right sterno-mastoid. In looking to the right we contract the right external and left internal rectus, *i.e.* impulses pass through the right sixth nerve and the left third nerve, possibly from the left and from the right side respectively of the motor cortex, but more probably from only the left motor cortex, in which case we must suppose that certain nerve-fibres cross twice, once between cortex and bulbar nucleus and a second time between nucleus and nerve termination. That the mechanism is actually of this nature is indicated by the effects of cortical convulsions and of cortical hemiplegia upon the position of the eyes. Unilateral convulsions of cortical origin are accompanied by rotation of the head and eyes towards the convulsed side, *i.e.* away from the cerebral lesion. Thus a discharging lesion of the right motor cortex causes convulsions of the left side of the body with rotation of the eyes to the left. This is a '*conjugate deviation*,' and the fact is peculiar, inasmuch as we have discharge from the right side of the brain along the

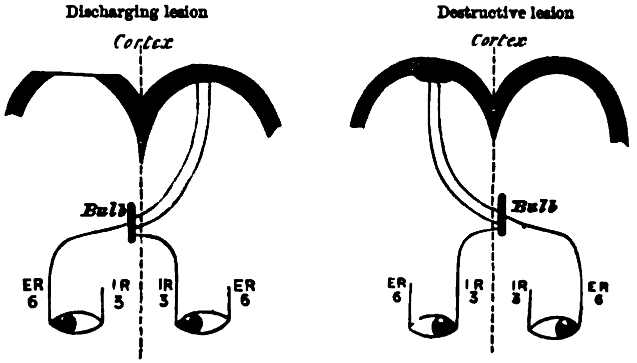


FIG. 269.

Diagram to illustrate conjugate deviation of the eyes—that is, *away from* a discharging lesion, *towards* a destructive lesion. In the diagram the eyes are supposed to be turned towards the left by a discharge from the right side of the cortex; to the right by unbalanced action of the left side of the cortex if the right side is destroyed. (In both cases the head rotates to the same side as the eyes.)

left sixth nerve (external rectus) and the right third nerve (internal rectus).

A destructive lesion of the right motor cortex causes paralysis of the left side of the body, with rotation of the eyes to the right. The peculiarity in this case is that there is cessation of action along the left sixth nerve (external rectus) and the right third nerve (internal rectus), the deviation of the eyes to the right being caused by the unbalanced action of the muscles which rotate the eyes to the right.

Movements of the eyes to the right or left are habitually associated with rotation of the head and neck in the same direction. The head is turned to the right by the left sterno-mastoid and right inferior obliquus capitis, and vice versâ; these, then, are conjugate muscles, acting like the eye muscles, above considered, and in conjugate action with them. This conjugation is preserved in the spasmodic or paralytic deviations caused by cerebral lesions; the head and neck being always turned in the same direction as the eyes.

Cortical Localisation

The physiology of the brain has since the year 1870 been engrossed by the one question of localisation. Is there a localisation of different functions in different parts of the brain, are its different parts concerned with different offices, is there a division of cerebral labour? or does every part subserve every office, can any office be administered by any part? To these questions it may be answered at once that the balance of evidence is in favour of localisation, but that the counter-evidence has shown that localisation is not sharply defined, but blurred. The state of doctrine may be made plain by an analogy. The various activities making up the business of the brain do not all take place all over its surface, as in a country without towns or villages, where all kinds of industry go on in every hut or tent: nor are the different activities absolutely restricted to certain spots, as if in walled towns. The brain cortex is not comparable with either of these extreme cases; its territory must be recognised as possessing towns with special industries, but towns with straggling and overlapping suburbs, and industries which are indeed predominant each in a given centre, but not exclusive of all other industries in that centre, nor excluded from other centres in which other industries predominate. In this qualified sense localisation of function in different parts of the brain must be considered to be established.

The chief facts by which the doctrine of localisation has been formed have been—

(1) The proof given by Fritsch and Hitzig in 1870 that the cortex of the brain responds to experimental stimulation, and that the excitation of certain different spots provokes certain different muscular movements; (2) the consequent detailed study by Ferrier, Munk, Schäfer, Horsley, Exner, Nothnagel, Beevor, Goltz, Franc, Heidenhain, Luciani, Tamburini, Seppilli, Löb, and many others, of the relation between cortical areæ destroyed or stimulated, and resulting muscular paralysis or spasm; (3) the scientific clinical study of epilepsy by Hughlings Jackson, completed by post-mortem recognition of the seats of lesion; (4) the association found to exist between aphasia and lesion of the left third frontal convolution.

The cortex of the brain is experimentally excitable.—This simple proposition was established by Fritsch and Hitzig in contradiction of the heretofore universally accepted statement by Flourens, Magendie, Longet, and the older physiologists, to the effect that the surface of the brain may be lacerated, pricked, burnt, mechanically, chemically, or electrically excited, without provoking muscular contraction in any part of the body. Fritsch and Hitzig used dogs, exposed the surface of an entire hemisphere, and tested it by interruptions of the constant current and by induced currents; they found the lateral and posterior parts of the cortex to be non-excitable, but in the frontal region they found certain spots, stimulation of which produced combined movements of the anterior or of the posterior extremities, of the neck, and of the face on the opposite side of the body; they found that on closing or reversing the constant current the anode was more effectual than the kathode, and they observed epileptic attacks following repeated stimulation and originating in spasms of the previously excited muscles.

Objections.—The electrical excitability of the cortex, the keystone of the doctrine of localisation, was not at once admitted as proved. It was objected that the diffusion of currents in the brain substance is such that stimuli cannot be limited to given areæ, and that the effects are due to the excitation of the subjacent white matter or of the basal ganglia. To this objection the answers

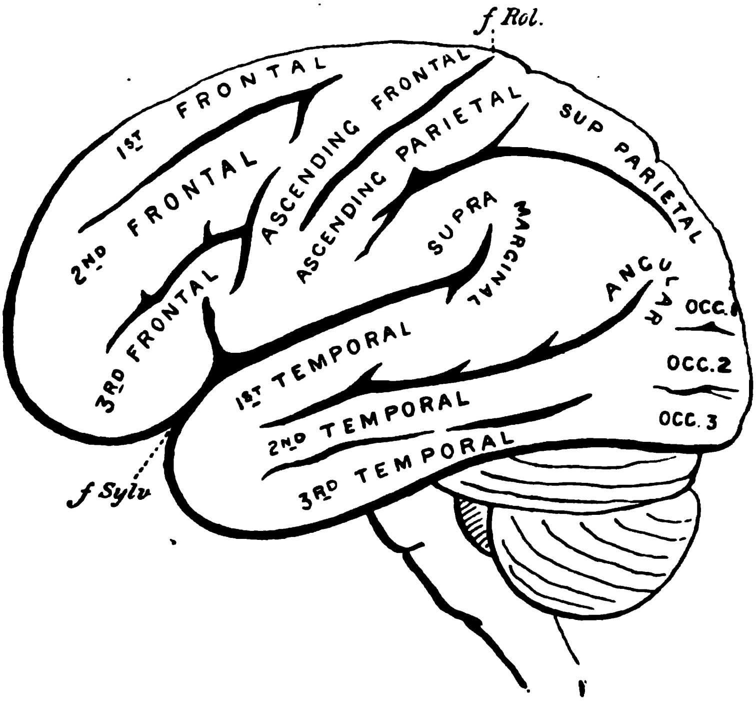


FIG. 270.—HUMAN BRAIN; LATERAL ASPECT OF LEFT HEMISPHERE. (After Ecker.)

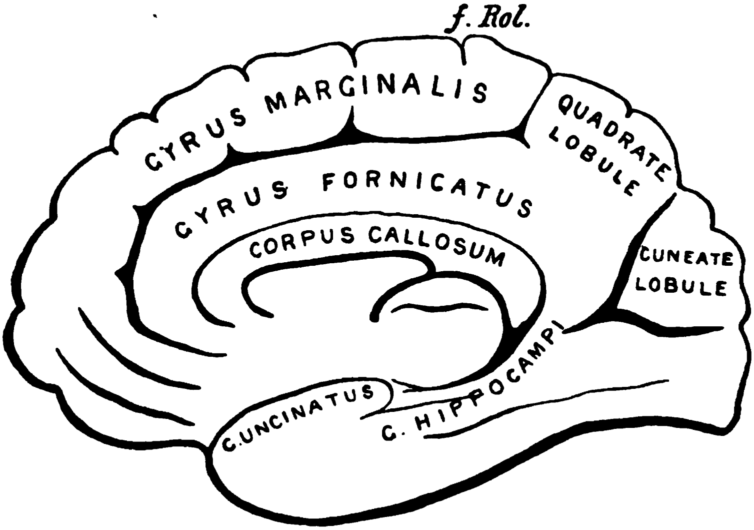


FIG. 271.—HUMAN BRAIN; MESIAL ASPECT OF RIGHT HEMISPHERE. (After Ecker.)

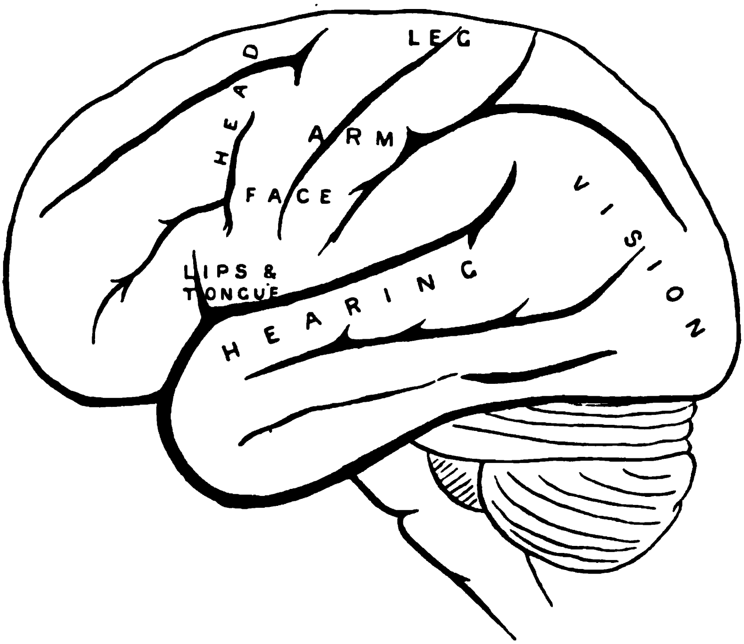


FIG. 272.—HUMAN BRAIN; LATERAL ASPECT OF LEFT HEMISPHERE. TO ILLUSTRATE CORTICAL LOCALISATION OF FUNCTION.

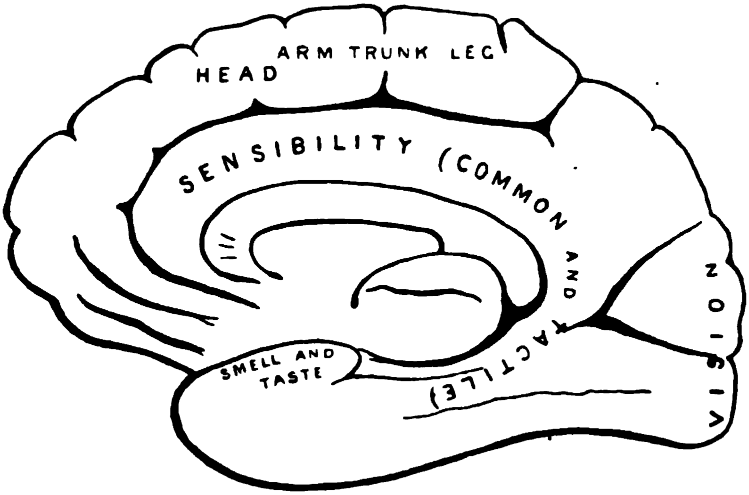


FIG. 273.—HUMAN BRAIN; MESIAL ASPECT OF LEFT HEMISPHERE. TO ILLUSTRATE CORTICAL LOCALISATION OF FUNCTION.

are: (1) No doubt the corona radiata is excitable; a localisation of effects is in fact demonstrable by excitation of different bundles from the cortex, as well as of different parts of the cortex itself; cortical stimulation remains without effect if the cortex is separated by an incision parallel to the surface, and replaced *in situ*; electrical diffusion to deeper parts is unaltered, but the physiological connection between cortex and base is interrupted. (2) Stimulation of the island of Reil, which is much closer to the basal ganglia than the Rolandic area, remains without effect. (3) Localised reactions are obtainable by mechanical stimulation of the Rolandic area. (4) Comparison of the 'lost times' in the two cases, viz. excitation of cortex and of subjacent white matter, reveals the fact that time is occupied in the physiological transmission of stimuli through the cortex; Franc and Pitres found for example on the dog, that the contraction of the front paw commenced ·065 sec. after a cortical stimulus, ·045 sec. after a stimulus to the subjacent white matter; *i.e.* they obtained ·02 sec. as the time-value of cortical delay. These results were confirmed by Bubnoff and Heidenhain, and supplemented by a still more convincing proof of cortical excitability. They showed that the muscular contraction obtained by cortical excitation of a morphinised dog follows after a much longer interval, and is much more prolonged than that obtained immediately afterwards by sub-cortical excitation.

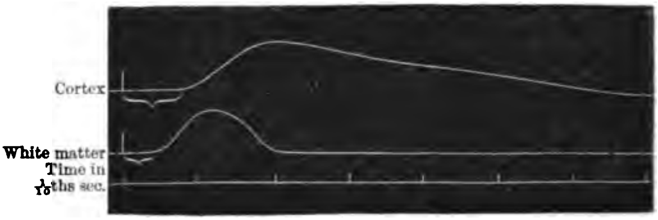


FIG. 274.—MUSCULAR CONTRACTIONS PROVOKED BY CORTICAL AND BY SUBCORTICAL EXCITATIONS. (Bubnoff and Heidenhain.)

The investigation opened up by Fritsch and Hitzig was soon afterwards pursued and extended by Ferrier (1874–78), who employed monkeys, and tested the cortical excitability by weak induced currents. He distinguished between direct and reflex excitability by differences in the character of motor reactions, regarding the reactions obtained by stimulation of the Rolandic area as direct motor reactions, and those obtained by stimulating the temporal and the occipito-angular areæ as reflex reactions, such as might be expected in consequence of auditory or visual sensations. Excitation of the left occipital lobe causes conjugate movement of the two eyes towards the right—*i.e.* 'the eyes turn, as if an object on the right, casting its image upon the left halves of the retinæ, had created an impression in the left occipital lobe.' In harmony with this view Schäfer finds that the latent time of the ocular movements is greater to stimulation in the occipital (or visual) area than to stimulation in the frontal (or oculo-motor) area. Ferrier found that direct excitability is limited to the convolutions in the vicinity of the fissure of Rolando, viz. the ascending frontal and ascending parietal. This region he therefore designated as the '*motor area*' of the cortex; and it may be remarked in this place that Ferrier's experimental results on monkeys are in general agreement with the deductions that Hughlings Jackson had previously made by the clinico-pathological study of epilepsy in man—to wit, that combinations of muscular movements originate in the middle region of the cortex of the brain. Ferrier, moreover, sought to localise the position of sensory centres by observing the sensory defects consequent upon the destruction of different cortical areæ; he came to the conclusion that *vision* is represented in and near the angular gyrus, *hearing* in the first temporal convolution, *smell, taste, common and tactile sensation* in the hippocampal region. But a localisation of sensory regions—assuming that sensory impressions, like motor impulses, are centrally differentiated—is a far more uncertain question than the localisation of motor regions; the margin left to be interpreted—by opinions, or by fancy, or under the influence of preconceived theory—is very large, and consequently many different opinions have been and are held concerning sensory areæ. Munk, who subsequently investigated this aspect of the question (1877), placed vision in the occipital region; operating on dogs and on monkeys, he found that destruction of the cortex of both occipital lobes caused total blindness, destruction of one occipital lobe caused hemiopia on the same side of the retinæ, conjoined with impaired vision of the whole of the opposite eye. These facts are in agreement with the clinical symptoms observed in man; hemiopia sometimes coexists with hemiplegia, and in such case the patient cannot see to his paralysed side. If, for instance, the left hemisphere is at fault, the muscles on the right and the retinæ on the left are paralysed, and the right side of the field of vision is blotted out; moreover the impairment of vision is greatest for the right eye. Ferrier, in a subsequent series of experiments on monkeys, carried out in conjunction with Yeo, came to the conclusion that the angular gyrus *and* the occipital region are necessary to vision. They state that 'the only lesion which causes complete and permanent loss of vision in both eyes is total destruction of the occipital lobes and angular gyri on both sides,' and that destruction of the occipital lobe and angular gyrus on one side causes temporary amblyopia (=dulled vision) of the opposite eye and hemiopia of both retinæ on the same side as the lesion.

With regard to hearing, Munk was of opinion that the whole of the temporal region is its sensory area. Ferrier and Yeo reaffirm the conclusion that destruction of the first temporal convolution on both sides causes complete and permanent loss of hearing, and that entire destruction of the hippocampal region (hippocampus major and gyrus hippocampi) and neighbouring inferior temporal region causes complete anæsthesia of the opposite side of the body. On the other hand the statement that the temporal region is auditory, is formally contradicted by Schäfer, who found no impairment in the hearing of monkeys for weeks after complete destruction of that region, as verified *post mortem*. We must therefore suspend our opinion with regard to the cortical locus of the sense of hearing.

With regard to *common* and *tactile sensation* we are in presence of Ferrier's statement, that complete anæsthesia of the opposite side is produced by destruction of the hippocampal region, and of Schäfer and Horsley's statement that hardly any alteration of sensibility is produced by such lesion, while 'any extensive lesion of the gyrus fornicatus is followed by hemianæsthesia, more or less marked and persistent.'

As for *smell*, we can only—in the absence of satisfactory experimental or clinical data—point to the possibility suggested by comparative anatomy; the olfactory lobe and the hippocampal gyrus (uncus) are in anatomical connection, and their greater development has been found to be characteristic of animals with a highly developed sense of smell.

To recapitulate the main results in their order of certainty—

It is proved that the cortex is experimentally excitable.

It is proved that the Rolandic area is 'motor.'

It is proved that the occipital area is visual.

It is possible that the limbic lobe (Gyrus fornicatus et hippocampi) is in part or wholly a sensory area.

It is possible that the temporal area is auditory.

Subdivision of the 'motor' area.—The Rolandic area has been further subdivided by experimental stimulation into parts which are found to be connected with definite groups of muscular movements of the upper or lower extremities, of the face, neck, or trunk. To the localisation thus determined the same qualification applies as that which we recognised in the general question: viz. localisation is not strict but straggling; there is no exclusive connection between points of cortex and parts of muscle, but a predominant connection between cortical regions and associated or grouped voluntary movements.

On the external aspect of each hemisphere the chief motor loci are as follows:—

Movements of the—

Inferior extremity	Upper portion of Rolandic area
Superior extremity	Middle portion of Rolandic area
Face	Lower portion of Rolandic area
Lips and tongue	Base of third frontal convolution
Head and eyes	Base of first and second frontal convolutions

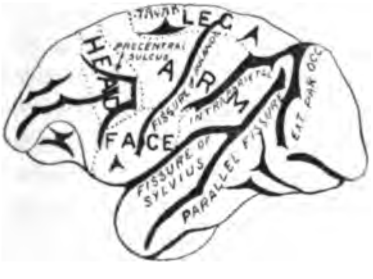


FIG. 275.—LATERAL ASPECT OF MONKEY'S BRAIN TO ILLUSTRATE CORTICAL LOCALISATION. (Horsley and Schäfer.)

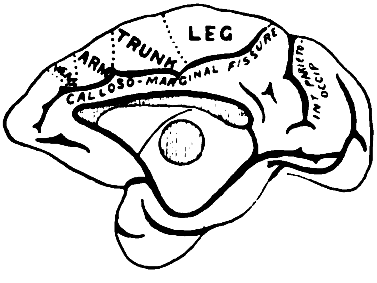


FIG. 276.—MESIAL ASPECT OF MONKEY'S BRAIN TO ILLUSTRATE CORTICAL LOCALISATION. (Horsley and Schäfer.)

On the mesial aspect of each hemisphere, *i.e.* in the marginal gyrus, the disposition is as follows from before backwards: head, arm, trunk, and leg.

By carefully localised stimulation a still further subdivision of areæ is possible, particularly in the case of that of the upper extremity. Particular movements of the arm, forearm, hand, and thumb can be produced by excitation of particular spots 'almost as regularly as definite notes can be sounded on a piano by touching particular keys.'

According to Ferrier and Yeo a similar localisation is repeated in the case of individual motor nerve-roots; these do not contain nerve-fibres to all sorts of muscles, but groups of fibres which are functionally associated, inasmuch as they supply muscles which habitually act together; stimulation of a nerve-root does not cause confused 'anyhow' muscular contractions, but a definite co-ordinate movement or manœuvre.

Subdivision of the visual area.—Munk and more recently Schäfer have taught that different parts of the retinæ are in functional connection with different parts of the visual area of the cerebral cortex, the retina being as it were 'projected' upon the occipital region of the opposite side, so that the upper retinal segment corresponds with the antero-occipital area, the lower retinal segment with the postero-occipital area, the central spot of the retina with about the centre of the occipital area. Schäfer, while supporting the general doctrine of cortical projection, describes it somewhat differently; he considers that the visual areæ of the two sides overlap in such a way that the central spots of both retinæ are projected together near the middle line, while each occipital lobe, right and left, represents, as stated by Munk, the left and right retina. Ferrier considers that the 'angular gyrus is more particularly related to the area of distinct vision,' *i.e.* the macula lutea of the opposite side.

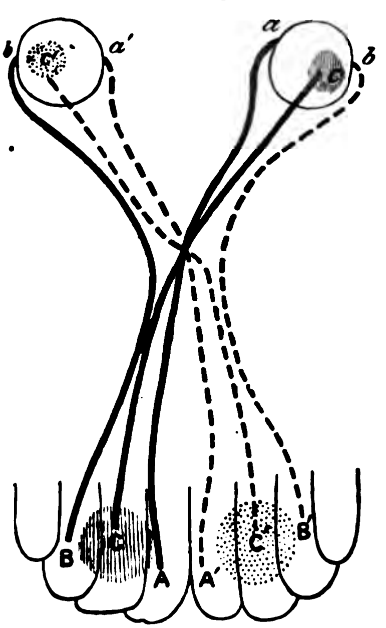


FIG. 277.—OCCIPITO-RETINAL CONNECTIONS ACCORDING TO MUNK, FROM EXPERIMENTS ON DOGS AND MONKEYS.

Each occipital lobe A B C is connected with *a* and *c* of the opposite retina, and with *b* of the same side. (Section of one optic nerve gives degeneration in the opposite optic tract towards A and C, and in the same side tract towards B′, not reaching higher than the anterior corpus quadrigeminum and pulvinar.) (v. Gudden.)

Of the many ingenious schemata which have been proposed to illustrate the connection between retina and cortex, that of Munk gives the clearest and most probable view, and is in harmony with our knowledge of optic-tract degenerations. It exhibits, as the main consequence of lesion of the occipital cortex on one side, paralysis of the opposite sides of the two retinæ, most pronounced in the opposite eye. Subsidiary features of the view held by Munk with regard to the cortical representation of the yellow spot, &c., are, however, very problematical. He considers that in each occipital area three regions may be distinguished—an internal region A, connected with the nasal half of the opposite retina; a middle region C, connected with the yellow spot of the opposite retina; and an external region B, connected with the temporal half of the retina on the same side.

Epilepsy.—The minute study of epileptic spasms has contributed largely to our knowledge of cerebral mechanism. Clinically the form of epilepsy which most nearly concerns the physiologist is that known as Jacksonian, or cortical epilepsy, which has a closely similar counterpart in the epileptoid attacks produced on animals by experimental stimulation of the cortex. A typical epileptic fit of cortical origin is divisible into the definite stages (1) of the warning sensation or aura; (2) the fit proper, or period of excessive muscular discharge; and (3) a post-epileptic stage, characterised by muscular debility, which may amount to actual paralysis, and which is referable to an exhaustion of 'discharged' cortex. The entire phenomenon is comparable to a protracted series of explosions, arising in an over-irritable or definitely irritated spot of the cortex as its focus of origin. The character of the warning and the mode of commencement of a fit give a clue to the actual seat of irritation; the order of invasion and the character of the convulsion are the outward sign of the directions along which the original cortical disturbance has spread. The warning sensation may consist in a peculiar sensation in the muscles of the limbs in which the convulsion is about to commence, or it may take all kinds of subjective forms, from a simple flash of light, or a sound, smell, or taste, to an elaborate representation of scenery or of music. Such muscular, visual, or auditory auræ, if well characterised, are to be taken as symptoms pointing to the area within which irritability is overstepping the boundary line into actual irritation. The fit proper—clinically divided into a short tonic period, during which muscular contraction is at its height, and a longer clonic period, during which muscular contraction is resolving itself—is significant of excessive discharge from the motor area of the cortex. Physiologically the feature of greatest interest is the order in which the limbs become affected at the very commencement of the fit. It may commence in any one limb; ordinarily it does so by twitchings of the highly specialised extremities most used in voluntary movement, viz. the thumb and fingers, and thereafter involves the forearm and arm, the opposite upper extremity, the face, and finally the lower extremities. But the order of invasion is by no means invariable. The part first invaded does, however, furnish valuable hints towards determining the precise seat for operative interference in cases where there may be reasonable hope of cure by removal of irritation: a fit beginning in the left great toe would point to a discharging lesion of the upper part of the right Rolandic area; a fit beginning in the right hand would point to a discharging lesion about the middle of that area.

The variability of the order of invasion deserves attention; we are naturally led to inquire whether the diffusion occurs in the cortex, or in subordinate bulbo-spinal centres. The answer to this question is that the diffusion probably occurs in the cortex *and* in subordinate centres. Or there may be no diffusion, the epileptoid spasms remaining limited to a single limb, or to one side of the body, as a monospasm or as a hemispasm.

The phenomena of experimental epilepsy confirm this interpretation and fix it in certain particulars. An epileptoid attack remaining locally restricted, or taking place as the prelude to a general convulsion of the body, is apt to occur whenever experimental stimulation of the Rolandic area is at all prolonged or strong; the attack occurs or begins in the limb or part functionally connected with the particular cortical area excited; and if it become generalised the order of invasion is, as in clinical cases, a variable one. Its more usual but by no means regular order is—supposing the spasm to begin in the right upper extremity —as follows: right upper extremity + right lower extremity + left lower extremity + right upper extremity, *i.e.* the invasion is longitudinal before it is transverse. This order favours the view that the diffusion has occurred in the cortex of one side rather than in the spinal cord, where, as we have seen, diffusion of reflex stimuli is transverse before it is longitudinal.

The great part played by the cortex in the extension of an epileptoid storm is, moreover, demonstrated in the experiments of Munk and of Heidenhain. Munk arrested the partial epilepsy which he had excited in a single limb by rapidly excising the cortical seat of commotion. Heidenhain went further, and in an early stage of a general epileptic attack, put a single limb to rest by excising the cortical area by which it was governed. According to all experimenters no epileptoid attack can be produced after destruction of the cortex of both hemispheres.

But the doctrine that epileptoid diffusion is *exclusively* cortical, is not justified by further experiments. (1) Epileptoid convulsions may extend to parts of the body after removal of the cortex which is in relation with them. In this case the storm provoked in uninjured cortex, has involved subordinate centres, and has there become diffused. (2) Epileptoid convulsions may be provoked by stimulation of white matter after removal of the overlying cortex. In this case excitation of white matter has reached uninjured grey matter through commissural fibres, and there provoked a storm which has become diffused in subordinate centres. These points will be appreciated by following the lines of the diagram.

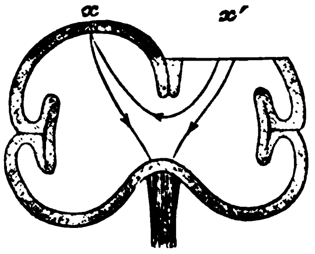


FIG. 278.—EPILEPTOID DIFFUSION.

The motor cortex of the left hemisphere is removed. (1) Stimulation x of the motor cortex on the opposite side has provoked an epileptoid attack; diffusion must have taken place in the bulbo-spinal grey matter. (2) Stimulation x' of the exposed white matter from the motor cortex of the left hemisphere has reached the right hemisphere through the corpus callosum and has provoked an epileptoid attack, which has arisen in the right motor cortex and must have diffused in the bulbo-spinal grey matter. (3) No epileptoid attack could be produced by stimulation of white matter after removal of the motor cortex on both sides.

Aphasia—literally loss of speech, more precisely loss of language—is one of the consequences of cerebral disease, and the discovery that such disease usually involves the third frontal convolution of the left hemisphere, was the first definite step in the localisation of cerebral diseases and of cerebral functions. The minute analysis of the various forms and symptoms of aphasia is thus a most important source of information in the study of cerebral mechanism. The subject of aphasia in its most typical form, is unable to express ideas correctly in words, either spoken or written, and this inability may be of any degree, from a transient or occasional misuse of a word, such as most people have experienced after hard mental work, to an habitual misuse of words or to their complete loss. Such an affection is termed *motor aphasia*, and its subject, though possessing ideas, cannot emit them for want of words, or emits them in wrong words: the ideas have no clothes to go out in, or they go out in the wrong clothes.[1] It is this form of aphasia which has been found associated with disease of the left third frontal convolution.

The term aphasia is also applied to a form of the disease in which the patient can express ideas in monologue, but cannot answer questions, this inability being due to the non-recognition of the words which he hears spoken or sees written. The defect may vary in degree from a transient absent-minded pause, such as occurs in the experience of most people, to the complete blank non-recognition of words. Such an affection is termed *sensory aphasia*, and is often spoken of as *word-blindness* or *word-deafness*, according as its subject fails to recognise words by sight or by sound. This form of aphasia has been found during the last fifteen years associated with disease of the optic or auditory regions of the cortex, *i.e.* of the occipital or of the temporal regions. The condition of a man the subject of sensory aphasia is strictly comparable with that of a dog from which the cerebral cortex has been removed: the aphasic man can see objects and hear sounds, but cannot recognise the meaning of written or of spoken words; the dog likewise can see and hear, but does not recognise the idea of a bone placed before him, nor the idea of the crack of a whip; he exhibits neither desire of the one nor fear of the other.

Let us follow the steps by which a rational answer is given to a question. (1) The subject must hear or see a word or words. (2) The word heard or seen must excite an appropriate sensory idea. (3) The sensory idea must give rise to a consequent motor idea, *i.e.* a word or words. (4) The word must be spoken.

No answer will be given if the subject be deaf or blind (1), or dumb (4); he is not on that account said to be aphasic. But he is so if he has no word with which to dress his outgoing idea (motor aphasia). Destruction of the third left frontal convolution, where his ideas are dressed, or destruction of the motor fibres from this convolution, causes such wordlessness. The destruction may be actual or functional, complete or incomplete: if incomplete the symptom will be incomplete; ideas few or many will be sent out dressed in wrong words. Again, he is aphasic if he cannot recognise the words in which another man's ideas are expressed (sensory aphasia), and theoretically he will also be aphasic if communicating channels be interrupted between the sensory, visual, and auditory regions and the motor or word region proper.

---

[1] A word is a complex bundle of movements—of the tongue and lips in *speech*, of the hands in *writing*, of various limbs in the *pantomime* sometimes used to denote mental ideas and to form propositions.

The study of aphasia further informs us in certain other important particulars. Aphasia is commonly associated with *right hemiplegia*, the common cause being obstruction of the left Sylvian artery. Aphasia due to this cause is generally of a mixed character, compounded of motor and of sensory symptoms, *i.e.* defects of emission (motor aphasia) and defects of recognition (sensory aphasia). The right Sylvian artery is seldom blocked, but when it is, left hemiplegia is its consequence, and aphasia is absent, except in rare cases, and it is said that most of these rare cases have occurred in left-handed people. These several facts go to show that the left side of the brain is normally the leading side not only as regards motion on the right side, but also and more so as regards speech; but that, as an exception, this precedence may be reversed, the right side of the brain being the leader, giving superiority to the movements on the left side and taking charge of speech.

The cortical centre of the closely associated function of vocalisation coincides with that of word emission, but in this case the centre is apparently bilateral—excitation on one side of the brain giving vocal movements on both sides, and destruction of both frontal lobes being necessary before these movements are abolished.

Recovery.—Aphasia may be permanent or may gradually fade away; a patient, speechless during the first few days after seizure, slowly recovers the use of proper language, and if the lesion have not been too profound, his recovery may to all appearance be complete. To explain this fact. In most cases it is doubtless due to restored circulation and nutrition. But in others we are compelled to believe that the right side of the brain gradually takes up the duty which normally belonged to the left side. The sensori-motor apparatus concerned in the perception and expression of language, holds on the left side as compared with the right a functional rank which is analogous with that held by captain and lieutenant; normally the latter acts in agreement with and upon the initiative of the former, but may on emergency succeed to and carry out the initiative action, which normally belonged to the leader. In other cases again, *i.e.* when aphasia is attributable to destruction of communicating channels between the left frontal gyrus and subordinate bulbar nuclei, it is possible that the rapid recovery which may occur is owing to the left side resuming action through the commissural fibres which form its communication with the opposite side of the brain.

The acquisition of language and its loss by *unilateral* cortical lesion illustrate a principle of far-reaching significance. Language is in the highest degree a special function, evolving last in the animal scale—taking form comparatively late in the individual life—most variable with varying education—first to show signs of failure in the degradation of cerebral function. The general functions and their organs are formed earlier than the special functions and their organs; the special functions and their organs are the first to fail in the dissolution of the formed organism. To use Hughlings Jackson's expression, language is a highest-level function; it comes last and goes first.

Deaf-mutes.—The modern or 'oral' education of deaf-mutes illustrates the acquisition of language under difficulties. In such people congenital deafness is the primary defect; muteness is its consequence, because the speech mechanism, although anatomically perfect, is deprived of education by sound, and remains undeveloped. In the place of articulate speech a deaf-mute employs a code of signals or intellectual pantomime for the exchange of ideas. Until within recent years this imperfect form of language was the only one taught; but it has been found that deaf-mutes can learn to recognise ordinary language, which they cannot hear, by seeing the lip-movements of a person who is distinctly articulating, and further that by close imitation of these lip-movements, they may learn to articulate distinctly in ordinary language. Such people learn speech by sight, whereas normal persons learn speech by sound, and the education of a person born deaf may be carried to such a pitch of perfection that the defect may pass unnoticed in ordinary conversation

In the foregoing account, and particularly in the short statements on p. 524, the terms motor and sensory are used in their ordinary sense, but 'without prejudice' and without implication of any theories with regard to the essential nature of the cortical processes so designated. It should however be added that opinions and interpretations of the intimate nature of the process, take very various shapes, and that inferences from facts are clothed in many kinds of verbal garments. Bastian interprets the results of excitation of the motor area as evidence that it is the central organ of muscular sense, and maintains that impairment of the muscular sense is associated with the impairment of motility caused by lesion of the Rolandic area. Flechsig, from entirely independent data, comes to the conclusion that the motor cortex is sensori-motor. Golgi, on histological grounds, comes to the same conclusion. Munk sees in his own results evidence that it is a sensori-motor area (*Fühlsphäre*); he finds that not only movements, but also sensations from the skin and from the muscles, are interfered with when portions of the motor cortex are extirpated. With regard to the occipital area, he distinguishes a central portion C, extirpation of which gives psychical blindness (*Seelenblindheit*), *i.e.* non-recognition of seen objects, from the surrounding portions A B, extirpation of which (added to that of C) gives total blindness (*Rindenblindheit*). (See fig. 277, p. 526.) In the temporal area he distinguishes a central portion, giving psychical deafness (*Seelentaubheit*), from a surrounding portion giving total deafness (*Rindentaubheit*).

The 'sensori-motor' conclusion is, indeed, an inevitable one; any motor or discharging centre must also be a sensory or receiving centre; it must be excited as well as excite. Any 'sensory' centre must also be motor, directly or indirectly; else we could have no objective tokens of sensation; every centre, whether called motor or sensory, is a *terminus ad quem* as well as a *terminus a quo.* Hughlings Jackson from the clinical standpoint particularly insists upon the 'sensori-motor' character of all centres as opposed to the crude conception of 'motor' centres, and in his hierarchical schema of central nervous mechanism represents sensori-motor centres in three grades —(1) highest-level centres (the prefrontal cerebral cortex), (2) middle-level centres (the Rolandic cerebral cortex), (3) lowest-level centres (the pons, bulb, and cord). This classification is practically the same as that which we have followed in the division into cerebral and spinal, with the additional subdivision of cerebral into upper and lower; and although pathologically the division may be legitimised by the analysis of epileptic and other phenomena, experimental physiology does not yet embrace these facts, nor recognise the distinction between supreme and subordinate cortex cerebri. But the actual localisation of three levels is quite secondary to their ideal conception; the contemplation of human conduct, normal and abnormal, fully warrants that conception, and it is of secondary importance whether the first two levels are both cortical, or whether one is cortical and the other subcortical.

Munk's conception is essentially similar to Jackson's, with the addition of an attempt at an actual localisation of two cerebral levels; but the terms he has used have obstructive connotations, and we should accept them more readily if they were more vague. If for *Seelenblindheit* we substitute 'high-level blindness,' for *Rindenblindheit* 'high + middle-level blindness,' we seem to understand better what is meant and what is the drift of the experiments in point.

The *reaction time* is the interval between the application of a stimulus and the responsive signal indicating that the stimulus has been '*felt*.' This interval is conveniently measured by arranging an electro-magnet to mark on a revolving cylinder (1) the moment when a tactile, auditory, or visual stimulus is applied, and (2) the signalling movement by which the person experimented upon indicates that he has felt the stimulus. The reaction time varies in different subjects, with different modes of stimulation, and with different degrees of attention and of health, between ten and twenty hundredths of a second. Average values of the reaction time are:

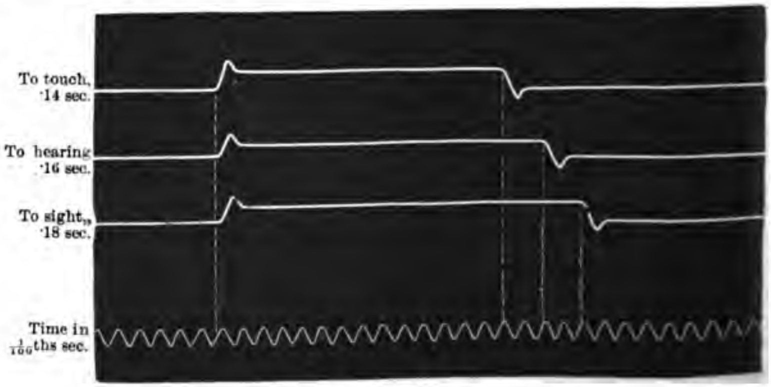


Fig. 279.

The total reaction time is composed of (1) the time occupied in conduction up sensory and down motor nerves, and (2) the time occupied in the central elaboration, during which entering impression gives rise to outgoing impulse. Thus in the simplest case, where the skin of the hand is stimulated by an induction shock and the signal given by the same or by the opposite hand, the interval (say ·15″) between stimulus and signal is made up of the time of conduction along sensory nerve (say ·02″) + the time of conduction along motor nerve and the muscular latency (say ·03″) + the time of cerebral elaboration, *i.e.* perception of sensation and formation of volition (say ·10″). It is the last of these three factors which varies most—with idiosyncrasy, attention, health, &c.—and it is partly on this account, partly because the sensibility differs at different parts of the skin, that measurements of the reaction time with cutaneous stimulation near and far from the head, give no admissible data for estimating rate of conduction along sensory nerves. The reaction time is shorter when attention is concentrated upon the intended movement than when it is concentrated upon the expected stimulus—this shows that the formation of volition involves more labour than the perception of sensation, the preparatory influence of attention being more effective if bestowed upon the outgoing than upon the incoming event.

With regard to individuality, it is not the case that persons reputed quick and 'wide-awake' have a shorter reaction time than persons of an apparently sleepy and phlegmatic temperament. 'Quick' people often have a long reaction time; 'slow' people often have a short reaction time; the relation, although common, is, however, not constant enough to constitute the rule. Experiments can easily be devised so as to yield an approximate estimate of the shortest time required to discriminate between two sensations (discrimination time) and of the shortest time required to determine an act of volition (volition time). For instance, the hand of a person, with bandaged eyes, on whom the simple reaction time to touch has been determined to be, say, ·15″, is stimulated on the little finger or on the thumb, with the understanding that only one of these stimuli is to be signalled; the reaction time is now found to be, say, ·17″, from which the conclusion is drawn that ·02″ was the discrimination time, *i.e.* that required to distinguish between the two different sensations. Or the experiment is conducted with two signals, on the understanding that one signal is to be used when the little finger is touched and the other when the thumb is touched; the reaction time under these conditions being found to be ·20″, is considered to be the sum of ·15″, the simple reaction time, + ·02″, the discrimination time, + ·03″, the volition time. The experiments may be still further complicated in a variety of ways, to measure the time of recognition of letters, words, simple ideas, &c., and are then distinguished by the title 'psychometric.'

Stimulation and sensation. The Weber-Fechner law.—Our measure of sensation being necessarily subjective, consists at best in the perception of the least observable difference between two sensations.[1] We assume that this least observable difference or differential sensation is a constant sensory quantity or one sensation unit; *e.g.* the differential sensation between two weights of 170 and 180 grammes, and the differential sensation between two weights of 1,700 and 1,800 grammes, are found by experiment to be 'least observable differences'—that is to say, equal sensations. Each such sensation is then assumed to be one unit, and in accordance with Fechner's exposition the assumption includes the differential sensation between zero and the smallest appreciable quantity of any stimulus—this minimum perceptible sensation being in fact the smallest observable difference between zero and something. This assumption is the basis of psychophysics. Within certain limits the strength of sensation increases with the strength of stimulation, and the relation is such that each equal increment of sensation requires an increasing increment of stimulation; *e.g.* a given sound of intensity = 1, producing a sensation = 1, must be increased to an intensity = $\frac{4}{3}$ before any difference becomes perceptible, to an intensity = $\frac{4}{3} \times \frac{4}{3}$ or $(\frac{4}{3})^2$ before a second difference is perceptible, to an intensity = $\frac{4}{3} \times \frac{4}{3} \times \frac{4}{3}$ or $(\frac{4}{3})^3$ for a third difference, to an intensity = $\frac{4}{3} \times \frac{4}{3} \times \frac{4}{3} \times \frac{4}{3}$ or $(\frac{4}{3})^4$ for a fourth difference, &c.[2] Thus the relative magnitudes of stimulus and of sensation will be expressed by the following numbers, or graphically by fig. 280:

---

[1] Nothing can be perceived otherwise than by comparison with something else, the most elementary sensation is the resultant of a *ratio* between *two* sensificatory terms $\frac{a}{b}$, and not that of a single term a or b. Something is perceived in comparison with nothing or with something else, and the resultant of the ratio in consciousness is a sensation. The highest forms of sensation are equally reducible to a ratio between *two* terms, each of which may, however, be a highly compound ratio.

[2] Sensation increases arithmetically, while stimulation increases geometrically; the equation to the curve, expressing their ratio, is $x = a^y$; *i.e.* the curve is logarithmic, and the sensation varies as the logarithm of the stimulus. Fechner's formula is $y = k \log \frac{x}{x_0}$, where y is the sensation, k a constant (differing with the nature of the sense organ), x the stimulus, and x_0 the liminal intensity (*reisschwelle*).

Sensation .	1	2	3	4	5	6
Stimulus .	1	$\frac{4}{3}$	$(\frac{4}{3})^2$	$(\frac{4}{3})^3$	$(\frac{4}{3})^4$	$(\frac{4}{3})^5$
or	1	1·33	1·77	2·37	3·16	4·2

Thus we may conceive that any
to a maximum by a series of equal
ceptible differences between its succe
from the first magnitude or mini
between nothing and something.

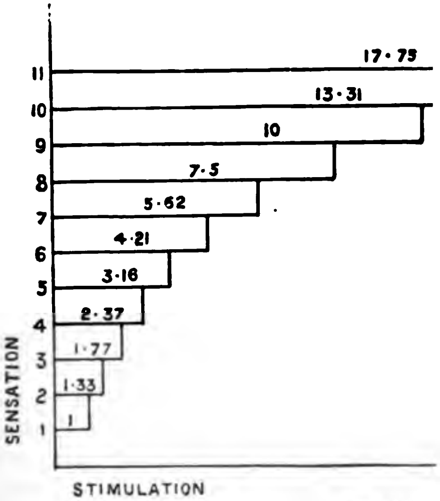


FIG. 280.

units are represented along the ordi
along the abscissa, we see the p
stimulation increments required fo
sensation increase. Otherwise ex
assumption that sensation units ma
magnitude, the relation may be pu
range the smallest perceptible differe
stant fraction of the original stimula
with different sense organs; thus for
ible difference is $\frac{1}{100}$, for *weight* it is
relation, known as Weber's law, is
experience, affecting every province o
limit to pains and pleasures, yet per
differences within a very extensive ran

Referring to the curve on p. 537, we see how rapidly a maximum of sensation is approached with increasing stimulation intensity, and a glance at the table on p. 539 shows us within what a wide range of light intensity we habitually live.

The most convenient stimulus with which to follow Weber's law experimentally, is that of light, and we shall describe how this may be done with very simple appliances, and in recollection of the physical law that the intensity of light varies inversely as the square of its distance.

Experiment.—Place a lighted candle at the distance of one foot in front of a vertical white screen in a darkened room. Let the illumination of the white screen represent unit intensity or 1. Take a second candle and any convenient opaque body, so as to obtain a shadow in the light from the second candle; move this candle away until the shadow is just perceptible or just imperceptible, and measure the distance, which is, say, 10 feet. From these data the minimum perceptible difference is easily calculated. The intensity of light from the first candle is 1, from the second candle $\frac{1}{10^2}$ or $\frac{1}{100}$; the shadow on the screen has an illumination from the first candle of 1, the unshaded portion has an illumination from both candles of $1+\frac{1}{100}$, *i.e.* the smallest observable difference is $\frac{1}{100}$th of the original candlelight. Repeat the experiment with a light of two candles one foot from the screen; the distance at which a third candle will give a shadow will be about 7 feet; the intensity of light in the just perceptible shadow is 2, and in the unshaded part $2+\frac{1}{49}$; *i.e.* the smallest observable difference is $\frac{1}{98}$, or about $\frac{1}{100}$. Repeat the experiment with a lamp replacing the two candles. Let us say that a shadow was just perceptible from a candle at 9 feet when the lamp was at 4 feet. The illumination of the candle at 9 feet is $\frac{1}{81}$th of the illumination of a candle at 1 foot. Assuming as a datum the previously determined fraction $\frac{1}{100}$ as representing the minimum perceptible difference, we have the illuminating power of the lamp at 4 feet$=\frac{100}{81}$ of a candle at 1 foot$=\frac{100\times16}{81}$ of a candle at 4 feet; *i.e.* the lamp-light is equal to that of nearly 20 candles. On the same principle we may approximately determine in terms of candle-power the intensity of diffuse daylight or of moonlight by observing the maximum distance at which a standard candle can cast a shadow on a white screen receiving daylight or moonlight. If in the first case that maximum distance were 2 feet, and in the second 110 feet, we should know that the value of daylight at the time was $\frac{1}{4}\times100$ or 25 candles; of moonlight $\frac{1}{12100}\times100$ or $\frac{1}{121}$ candle—assuming, as before, that the minimum perceptible difference was 1 per 100.

	Sensation units	Stimulation units	
Minimum perceptible . .	1	1	$\frac{1}{1000}$ candle
	11	1·1105	
	101	2·704	
	201	7·314	
	301	19·789	
Moonlight	• 370	40	$\frac{1}{100}$ candle
	401	58	
	501	144	
	601	390	
	701	1059	
	801	2865	
White paper lighted by candle at 1 foot	• 884	4000	1 candle
	901	7749	
	1001	20960	
	1101	56695	
	1157	100000	25 candles
	1201	158350	
	1301	414790	
	1388	1000000	250 candles
	1401	1121900	
	1501	3027900	
White paper lighted by sun .	1601	8208100	
Full sunlight	1701	22201000	5,555 candles

Sensory judgments, illusions.—Comparisons and judgments, unconscious as well as conscious, are performed in the brain, and consist in the collation and comparison of sensations, which may be simultaneous or successive. We shall refer, in illustration of this subject, almost exclusively to the sense of vision; it is the most important and most cerebral of the senses, and the most accessible to experimental analysis; but it should be remembered that channels of sensation other than visual convey sensations which are compounded in consciousness, and which supplement or correct visual and other judgments.

The popular expressions 'a correct eye,' 'sense of proportion,' are indicative of composite central qualities, partly inherited, partly acquired by education through the senses. It is not sufficient to possess sensory instruments; we must also be able to interpret their indications by cerebral inference. The simplest case to take in illustration of cerebral inference is the way in which we judge of the *size* of objects, and of their *distance* from the eye. The size we attribute to an object is the resultant of two factors, the actual size of its retinal image, the known or apparent distance from the eye. The distance from the eye at which we estimate that an object is situated is likewise the resultant of two factors, the actual size of its retinal image, the known or presumed size of the object. When we have a small retinal image of an object we know to be large, we judge it to be far off; when we have a large retinal image of an object we know to be small, we judge it to be close to the eye.

The standard of reference which we unconsciously or consciously employ in forming a conclusion from distance to size, or from size to distance, is the cerebral resultant of previously felt relations between size and distance—the personal ratio drawn from our stock of similar experience. Formally expressed, the major or general premise is our cerebral ratio of previous similar $\frac{\text{felt size}}{\text{felt distance}}$; the minor premise is one or other of these magnitudes in the particular case examined; if we make distance the minor premise, size is the conclusion drawn; if we make size the premise, distance is the conclusion. Or expressed as a proportion, a particular relation $\frac{s}{d}$ is compared with the general ratio $\frac{S}{D}$ by the unconsciously established equation $\frac{s}{d}=\frac{S}{D}$, with s as the datum and d as the conclusion, or *vice versâ*. Practically we carry out this proportion every day more or less exactly in our visual judgments. In any given case we form a cerebral minor premise by observation of a particular magnitude, we refer that premise to the standard of past similar experience as its cerebral major premise, and by inference form our cerebral conclusion. If, for instance, we have formed a cerebral datum from a retinal image cast by an object of known magnitude at an unknown distance, or of unknown magnitude at a known distance, we infer distance from size, or size from distance, more or less accurately according as our personal ratio between size and distance has been more or less accurately formed by previous training. A man who has been accustomed to express in numbers lengths which he has seen can put a more exact value upon the size of a house or field than a man who has not been so trained.

We are liable to be more or less grossly deceived by appearances. A man accustomed to hilly landscape will, if set down among mountains, overestimate size and underestimate distance. Having thus unconsciously prejudged magnitudes, he is surprised to find that men and cattle are not really smaller than usual, and that distances are much greater than he at first imagined. A hazy atmosphere makes hills look like mountains; a clear atmosphere makes mountains look like hills. An object seen through a telescope appears nearer than it really is, although on other grounds it is known to be at a great distance; conversely, an object looked at through a reversed telescope appears distant, although from other sensory information we know it to be near.

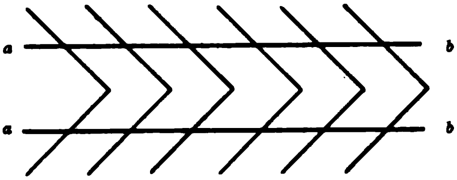


FIG. 281.—ZÖLLNER'S LINES.

Instances might be multiplied in which the cerebral representation of a given sensation is more or less altered by unusual sensory premises, or even irresistibly distorted by collateral sensations, but we shall only quote one such instance—that known as the Zöllner illusion. The two lines *a*, *b* are parallel; but in consequence of the inclination of the short lines crossing them they appear to diverge from left to right. In fig. 282 the two lines *a a*, *b b*, are of equal length, but in consequence of the short diverging or converging limbs *a a* appears longer than *b b*.

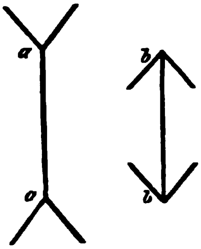


FIG. 282.

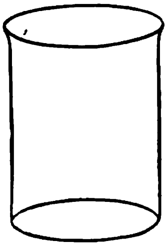


FIG. 283.

Finally we must allude to the fact that the cerebral representation of a sensation or group of sensations may, quite independently of any external distorting cause, be modified by the voluntary attitude and focalisation of attention. The figure of a beaker may be imagined and 'seen' at will with its open mouth either towards or from the observer; and an actual beaker can equally be 'seen' in either position, especially if one eye be closed to eliminate collateral items which correct and dissipate the illusion. This elimination is, however, not indispensable; even with both eyes open we may so forcibly focalise attention as to *see* erect a beaker lying on its side, or *vice versâ*, and *not see* the lights and shadows and perspective which antagonise the illusion. This simple experiment is thus illustrative of a very important cerebral custom in the formation of judgments; *i.e.* we see what we attend to, we do not see what we do not attend to. We can wilfully persuade ourselves of a fictitious phenomenon by focalising deceptive data to the exclusion of corrective data; and finally, having formed our fiction, we may consistently use objective data in further distortion of the reality. This last capacity, which is more or less obviously manifested in every man's daily life, is admirably illustrated by the closer consideration of the beaker experiment. Taking a cylindrical beaker or lamp-glass, placed erect and seen as erect, or placed on its side and seen on its side, the vessel in each case seems cylindrical; but if by a forcible self-suggestion the observer 'sees' the erect beaker tilted away from him, the apparent near end looks narrower: or if he sees the overturned beaker as if erect, then the apparent upper diameter seems to be smaller; in each case the really cylindrical object appears to be conical; the observer having formed his false notion, makes further use of the real retinal magnitudes of the image conformably with that notion; in the first fiction the retinal image of the upper end is imagined to be more distant, and therefore appears larger; in the second fiction the further extremity is imagined to be nearer, and therefore appears smaller. The great power of this self-deceptive effort may be realised in its fullest extent by holding the beaker in front of the eye and tilting it in various directions; the movements may be 'seen' reversed at will, in spite of the muscular contractions which the observer is making to produce them.

There are reasons for thinking that the process of inference or judgment, as known to us by introspective analysis and characterised to be an exclusively 'cerebral' function, is also represented in simpler degree in the unconscious operations of subordinate centres, and that we may receive in a supreme centre the *resultant* of impressions already combined and elaborated in a subordinate centre. We have no positive knowledge of the actual seat of formation of particular inferences; they may be superior and inferior cortical, or cortical and subcortical; but this ignorance is no bar to the essential conception that such processes may occur at different functional levels. In the case of Zöllner's illusion the lower-level inference is so strong as to irresistibly elicit the higher-level inference; we *cannot see* the lines parallel, although we may *know* by measurement that they are so. In the series of beaker observations the lower-level inferences are formed from sensations sufficiently ambiguous to allow a higher-level inference to be formed, either rightly or wrongly, and if in that inference *one* of the lower-level components is misjudged, other lower-level components follow suit. With the erect beaker, seen so that the proximal edge appears to be behind the distal edge, that misjudgment of lower by higher inference carries with it misjudgment of the low-level inference from the retinal magnitude of the image. The image of the beaker-mouth is no larger than before, but the beaker is seen tilted away; therefore the low-level inference of size is exaggerated in the high-level compound inference of position *plus* size.

An important means of estimating the distance of objects is afforded by our unconscious appreciation of the difference between the two pictures formed on the two retinæ; this factor is especially important in our perception of the third dimension of space, and consequently of the form of solid objects. Length and breadth can be judged of with one eye open as well as with two, but to get the notion of depth we are much assisted by the double sensation of two slightly different pictures. An ordinary landscape looked at with both eyes open, appears much more extensive as regards the third dimension than when it is looked at with one eye shut. On the contrary, the painting of a landscape appears much flatter when it is looked at with the two eyes than with one only. These differences may easily be understood: the depth of a landscape is most apparent when two different retinal pictures are formed; the want of depth in a picture is most apparent when two identical retinal pictures are formed; it is especially the foreground effects which influence our judgment in the two cases.

In the more delicate discrimination of distance at closer ranges, *e.g.* when the hand is put out to move a piece at chess, other subjective factors connected with the muscular sense come into play, viz. the degree of convergence of the two visual axes and the amount of accommodation exerted. The value of these factors, as distinguished from the retino-cerebral factor, is, however, difficult to appreciate, and the attempt to do so would lead us too far.

The stereoscope and the telestereoscope are instruments so constructed as to give an exaggerated notion of the third dimension. In the ordinary stereoscope two photographic pictures, taken from slightly different points of view, are looked at each by one eye, and the visual axes are converged until the two pictures become 'identical' on the two retinæ, and therefore fused in consciousness as a single picture in which 'depth' becomes particularly apparent. This is called a 'stereoscopic effect,' and in the actual instrument the convergence of the visual axes is imitated and exaggerated by two prisms with the thick edge outwards, one in front of each eye. That 'stereoscopic effect' is not due to movements of the eyes is proved by the fact that it is produced by pictures illuminated by the electric spark; this illumination does not last more than $\frac{1}{4000}$ sec., a period during which no sensible movement of the eye is possible.

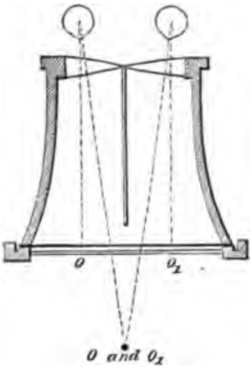


FIG. 284.—STEREOSCOPE.

Two objects, o and o_1, are viewed in conjunction. (Helmholtz.)

If, instead of placing in the stereoscope two photographs prepared *ad hoc*, we examine two identical pictures or prints, their two images give no stereoscopic relief, but combine into a single flat image. If there be the slightest difference between the two prints, this will at once be detected as an irregularity when they are combined by the stereoscope. Two genuine bank-notes can be thus perfectly combined; a genuine and a spurious note cannot.

The effect of the telestereoscope, as will be understood from the accompanying figure, is to exaggerate the difference between the two retinal pictures of a landscape by causing the points of view of the two eyes to be much farther apart than normal. The normal distance $l\ r$ between the centres of the two eyes being 65 mm., are by the telestereoscope increased to the distance

l_1 r_1. If, for instance, this distance be 65 cm., the normal stereoscopic effect is proportionately exaggerated, and at the same time

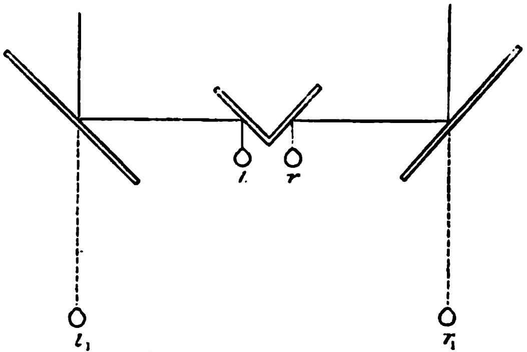


FIG. 285.—TELESTEREOSCOPE.

Two small mirrors in front of the eyes l r; two larger mirrors arranged to reflect images of distant objects upon the smaller mirrors and thus to the eyes. The effect is as if the eyes were placed at l_1 r_1. (Helmholtz.)

objects in the landscape appear reduced in size and produce the effect of stage scenery.

Contrast.—Any quality, optical or other, of an object or person causes in the observer an impression which is intensified if the surroundings are of an opposite quality, weakened if they are of a similar quality. Any given quantity is over-estimated when its surroundings are unusually small, under-estimated when its surroundings are unusually large. 'Rest can only be enjoyed after labour; sound, to be heard clearly, must rise out of silence; light is exhibited by darkness, darkness by light; and so on in all things.' Stated more generally, the value of any given constant is estimated to be + or − according as its surroundings are − or +. A person of average height appears taller among short people, shorter among tall people. If one finger dipping in hot water and another finger dipping in cold water be both simultaneously transferred to tepid water, the first finger will feel cold, the second warm; these are phenomena of successive contrast, analogous with the negative after-effects of visual excitation.

Formally expressed, if $\frac{A}{B}$ is the personal ratio or major premise, $\frac{a}{b}$ the minor premise formed by an object in its surroundings, then the object *a* varies inversely as the surroundings *b*; if by the focussing of attention *b* is made the premise, *a* becomes the conclusion, and *vice versâ*.

What is the nature of colour contrast? Two rival theories, one known as the psychological theory, the other as the physiological theory, are still upheld by two different schools. The first or psychological theory is that of Helmholtz, and represents contrast as being an error of judgment; the second or physiological theory is that of Hering, and represents contrast as due to the up-and-down chemical modifications of a hypothetical retino-cerebral 'vision-stuff.'[1] According to his mode of expression, an opposite or assimilatory change (black, blue, or green) is induced in the surrounding area, if a direct or disassimilatory change (white, yellow, or red) be provoked in a given area—and *vice versâ*.

We must first clearly define the issue: it is strictly limited to the phenomenon of simultaneous contrast, *i.e.* that produced with the 'fixed eye,' and to its after-effects.[2] The effects of successive contrast, which are attributable to fatigue, must be carefully excluded. The experiments upon which the debate has especially turned are (1) the experiment of coloured shadows and (2) Meyer's experiment (p. 449).

Helmholtz, in connection with the first experiment, urges the following points:—If one looks at the shadow of the candle-light through a tube, the round area is colourless, *i.e.* objectively there is no colour there. If the tube is directed so as to be half on the shadow, half on the adjacent area lighted by the candle, the shaded half looks blue. *If now the tube is turned back to the first position the whole of the round area continues to appear blue, even if the candle is put out; but the moment the tube is removed from the eye the blue spot vanishes.* 'No experiment shows in a more clear and striking manner the influence of judgment upon our colour determinations. As soon as we have judged the candle shadow to be blue, as a consequence of simultaneous or successive contrast, the colour apparently remains blue, even after the circumstance which has led us to that conclusion has disappeared, until the removal of the tube has allowed us to make a new comparison and caused us to make a new judgment.'

---

[1] It is not correct to apply 'retinal' to Hering's theory in opposition to the term 'cerebral' to designate Helmholtz's theory—for he expressly and repeatedly states that he uses 'retinal' as short for 'retino-optic-cerebral.' Nor is it correct to characterise the theory as 'photo-chemical,' and to conjoin it with the effects of light on the retinal purple; Hering expressly excludes this interpretation, and states that by vision-stuff he means an imaginary psychophysical matter forming and resolving itself under the influence of different kinds of light.

[2] The after-effect of simultaneous contrast is not to be confused with successive contrast; in the latter case a given area of a wandering retina is successively excited (*v.* p. 450), in the former we compare the simultaneous effects on each other of the two after-images.

Hering insists upon the necessity of most carefully distinguishing simultaneous from successive contrast, and objects to the conclusion quoted from Helmholtz, that the persistence of blue in the third step of the experiment is simply a phenomenon of successive contrast. Adopting a somewhat different arrangement, he steadily looks through the tube fixed so as to include a half-disc of shadow (blue) and a half-disc of gas-light (yellow). Keeping his eye upon the middle point of the disc, he pushes the shading body so as to shade the entire disc, and now the previously yellow half looks blue, and the previously blue half faintly yellow. Finally, he turns off the gas-light and removes the tube, still keeping the eye steady, and now he sees on the white field the negative after-image of the disc—the previously yellow half looks bluish, and the previously blue half looks yellowish.

Helmholtz's interpretation of Meyer's experiment is as follows: 'If the background is green the covering paper looks greenish. If the latter covers the grey scrap without interruption we fancy that a grey object is seen through a greenish veil; such an object, to look white, must be rose-coloured.'

But, says Hering—and the statement is easily verified—a chess-board pattern of grey and green squares, covered with tissue paper, over which a black paper with a square opening is placed, gives a similar if less pronounced effect; a person coming fresh to it, sees no covering paper, but merely a pattern composed of greenish and reddish squares.

We may make Meyer's experiment in a form which is still more unfavourable to Helmholtz's interpretation, by substituting for the grey paper a piece of the same tissue paper which is to cover the whole; without the cover the field is green and the patch greenish, with the cover the field appears greenish and the patch rosy, although we *know* that the patch is not white but greenish. On the other hand we may give to the experiment a form which is very favourable to the Helmholtz view, thus: A narrow strip of grey paper is placed on a white field; two rectangular pieces of coloured paper are fixed at each side of the strip, bordering upon the middle portion of its length; the whole is covered with tissue paper. The entire length of the grey strip appears of uniform greyness or very faintly tinged; but if the coloured rectangle is completed by white or black lines crossing the grey strip, the portion enclosed by these lines assumes the complementary tint, while the portions above and below do not, but, if anything, are slightly tinged in the same sense as the coloured paper.

Hering's view is that simultaneous contrast depends upon the fact that any excitatory disintegration of a retinal area is accompanied by a reverse alteration or integration of the surrounding neighbourhood, or *vice versâ*, causing a light halo round a dark patch, red round green, green round red, blue round yellow, yellow round blue.

Hering's fundamental experiment in support of this position in one of its simplest and most striking forms is as follows: Two V-shaped pieces of grey paper are placed upon white and black backgrounds, as shown in fig. 286. By contrast the V on the dark half looks lighter than the V on the light half. The point of fixation is steadily looked at for half a minute to a minute; the gaze is then removed to a point of fixation in a uniform surface. The previously dark half of the field looks light as compared with the previously light half; the after image of the previously lighter V looks darker than that of the previously darker V; and even when the contrast between the backgrounds has faded off the contrast between the two V's still remains perceptible. This after-difference must be due to localised change; it cannot be due to false judgments between each V and the corresponding background after-effects. The experiment can be varied with similar effects, to which similar reasoning is applicable, by taking coloured strips of paper on coloured backgrounds, *e.g.* yellow and blue strips on blue and yellow grounds respectively. The after-images of the strips contrast, even after

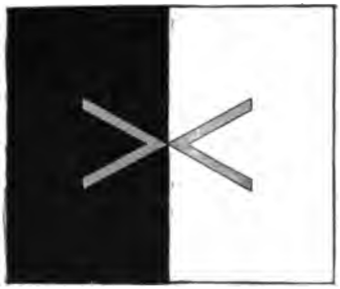


FIG. 286.

the background after-images have ceased to contrast. We may even arrange matters so as to obtain a strong simultaneous contrast between two areæ in which contrast colours are produced by coloured fields which are themselves in much weaker contrast: A white surface in front of the two eyes, with a red glass in front of one eye and a blue glass in front of the other, is red or blue to each eye respectively; a black strip on that surface, seen by both eyes open but not focussed for the strip, forms images on non-corresponding parts of the two retinæ, and the two apparent strips are in strong contrast, while the surrounding areæ appear respectively scarcely blue or scarcely red, and in much less striking contrast than the strips.

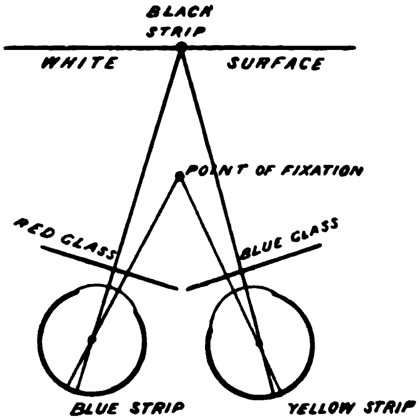


Fig. 287.

In sum, what are we to believe? Dogmatic faith is out of the question; still we may provisionally conclude that while 'misdirection of judgment' plays a part in a multitude of contrast phenomena, material alterations of the retino-cerebral apparatus are in cause in this particular class of contrast phenomena; and this fact being admitted suggests that similar alterations must also play a part in other sensory phenomena classed as 'psychological.' The Helmholtz-Hering issue in this connection is to the following effect:—Helmholtz holds that material sensificatory data do not directly modify each other, but that indirectly in the process of inference any datum will be reversely modified by any other datum in the field of perception. Hering urges that each material sensificatory datum diffuses beyond its precise locus of incidence, and thus directly modifies contiguous sensificatory data; without entering into lengthy developments we may recognise that Helmholtz's contention is borne out by many simple experiments, *e.g.* by the beaker observations described on p. 542, while Hering's mode of interpretation is certainly most applicable to the phenomena of simultaneous light and colour contrast.

The term 'judgment' belongs to psychology rather than to physiology, but in any account of the functions of the brain it is not possible to escape the use of terms bordering upon or actually belonging to the domain of psychology. We may take this opportunity of recognising one or two of the instances where this trespass has been unavoidably committed. 'Consciousness,' 'judgment,' 'sensation,' 'attention,' 'memory' are the principal terms thus involved; and although we shall fail to define them strictly, we shall with profit recognise the sense in which each term has been used in the present discussion. *Consciousness* is the subjective experience of each individual; we cannot physically describe the nature of the phenomena which it indicates; we simply paraphrase the term by saying that consciousness is the subjective aspect of objective material changes in the outside world and in the cerebrum of the conscious agent. *Sensation*—*i.e.* impression of which the subject is conscious—we have used in the sense of 'felt impression' in consciousness, without drawing, therefore, any distinction between a sensation and a perception. *Memory* is the consciousness of former material changes and sensations; objectively it is conceivable as the attribute of material cerebral alterations left by previous sensations—the 'organisation of past experience.' *Attention* and *inattention* are attitudes of consciousness, which is concentrated or not concentrated upon given objects. *Judgment* in its simplest form, or inference, is the resultant of compared sensations, a consciousness of their identity and of their difference, *i.e.* of their ratio; in its higher and more compound forms it is the resultant of compared ratios, *i.e.* of a synthetic process *in which the major premise is the personal ratio of the thinker.*

Fatigue.—Fatigue in the ordinary sense of the word is a sensation caused by previous exertion or prolonged excitation, and manifesting itself as blunted sensibility or diminished motility. From the physiological standpoint motor fatigue is recognised in a diminished energy of motion. We have already on more than one occasion referred to the objective signs of motor and of sensory fatigue (pp. 377, 448); we have now to disengage the shares of the total burden borne by central and by peripheral organs in the cases of voluntary action and of sensation. We may at once dismiss the latter; we have no means of separating a peripheral from a central factor in the case of sensory fatigue; all that need be said is that the minimum excitation and minimum perceptible difference between two stimuli must be larger in the fatigued than in a normal condition of any sense organ. As regards voluntary motor fatigue we can, however, by experimental means separately demonstrate, and to some extent measure, central and peripheral loss of energy. We saw in the section on muscle and nerve (1) that nerve is practically inexhaustible, (2) that the exhaustion of the motor end-plate precedes and obstructs exhaustion of muscle submitted to indirect excitation. The problem now before us is therefore limited to an appreciation of the distribution of motor fatigue in cerebral and in peripheral organs. The appreciation cannot be made precisely, but we may obtain definite evidence that peripheral and central organs both participate in the change. The mere sense of fatigue contains no proof at all; the material change might be central or peripheral, or both. But that it is in part peripheral is proved (1) by the beneficial effect of massage, (2) by the smaller amount of energy elicited by direct electrical stimulation after exhaustive voluntary action. That it is in part central is proved by the fact that when cerebral action has ceased to be effective on muscle, electrical stimulation of nerve or of muscle is still provocative of contraction. The following experiment may be quoted in evidence of central fatigue:—If a series of induction shocks is applied to a frog's brain and bulb until the gastrocnemius has ceased to respond, a second series of contractions may be elicited by switching the current to a pair of electrodes applied to the sciatic nerve; if when the muscle has ceased to respond to this excitation the current is switched to electrodes applied to the muscle, a third series of contractions is obtained; from which we learn that maximum action of the superior organ does not elicit maximum action of the subordinate organ—in other words, that central fatigue is limitative of peripheral fatigue—and we may formulate as a probable conclusion, that the incidence of normal voluntary fatigue is in diminishing gravity from centre to periphery—relatively greatest at the former, relatively least at the latter.

Sleep.—After exertion rest is necessary; expenditure of material during the former is made good by restoration during the latter. The brain conforms to this necessity, and does so in a periodic manner. But sleep is not an exclusive attribute of the brain; it extends in less degree to the subordinate nerve centres, and is attended with a diminished activity of the periphery itself, as evidenced in the slower respiration, slower pulse, diminished excretion of CO_2, diminished secretion of urine.

The state of the cerebral circulation during sleep has been the subject of some debate; opposite opinions have been advanced, to the effect that the brain is anæmic, or that it is congested. Although there is no doubt that in coma—a pathological state similar in some respects to physiological sleep—the cerebral vessels are congested, the observations of Durham on the exposed cerebrum of sleeping dogs, and of Jackson on the retinal vessels of sleeping infants, are to the effect that vessels shrink in sleep, and we may therefore feel reasonably assured that the sleeping brain, in common with other resting organs, receives less blood than in its state of activity. Moreover, Mosso's investigations on exposed human brains afford evidence that the organ becomes more vascular during mental activity.

On the supervention of sleep, external impressions cease to be perceived, consciousness fades, the voluntary muscles relax, the eyelids drop, the eyeballs turn up, the pupils contract. The time at and during which different persons sleep is liable to considerable variations, in accordance with temperament and habit; normal sleep lasts for six to nine hours, and it is best that these should be hours of darkness. An excited brain, unusual and irregular stimuli of any sense, are the usual causes of wakefulness; a moderately fatigued condition of 'mind' and body, quietude or monotony of surroundings, are favourable to the arrival of sleep. The depth of sleep is very variable; in deep sleep consciousness is absent, stimuli of even considerable strength may be insufficient to arouse sensation, the muscles are completely relaxed, the so-called tendon-reflexes are in abeyance, the deep sleeper lies dreamless and motionless. All these signs are wanting in sleep which is light, or partial: consciousness is

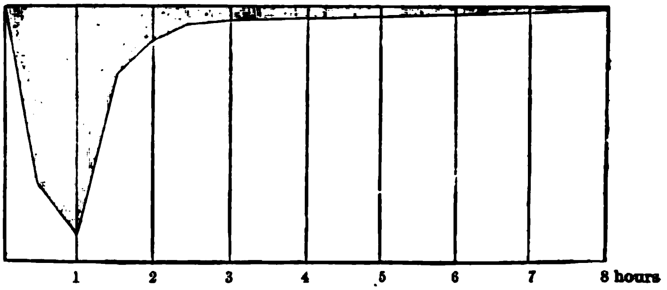


FIG. 288.

To illustrate the depth of sleep as investigated by the loudness of sound required to wake the subject. (Exner after Kohlschütter.)

blunted but not absent; ideas string themselves together in more or less congruous sequence and form dreams, or are aroused by more or less appropriate stimuli, or they actually arouse movements more or less coordinate and purposive, such as are seen in their fullest expression in the actions of sleep-talkers and of sleep-walkers. Normally a sound sleep is deeper at its commencement than at its end, though abnormally it often happens that a wakeful person sleeps partially and insecurely at first, heavily and deeply later on. The accompanying curve, in which the shaded ordinates represent intensities of sound sufficient to awaken a sleeping person at different periods, gives an idea of the normal depth of sleep from the first to the eighth hour.

Hypnosis.—It is not possible at the present day to conclude an account of the action of the central nervous system without reference to the phenomena of hypnosis.

It has long been known that a condition which we now call 'hypnotic' is inducible in animals. Kircher's *experimentum mirabile*, consisting in placing a fowl with its beak to the ground before a chalk line traced from it, is one of the first on record (1646). Many birds, mammals, amphibia, and reptiles are hypnotised by simply turning them on their backs, their condition being doubtless attributable to a sense of helplessness or fear; the phenomena of fascination by snakes are of a similar character.

The hypnotic state in the human subject presents many features of resemblance with normal sleep, but with this great difference, that whereas a person in natural sleep has no specific differences of susceptibility towards the items comprising his environment, the hypnotised person has been influenced by the action of the so-called 'operator,' and remains specially susceptible in that quarter, while less susceptible in all others: he is '*en rapport*' with the operator.

An ordinary sleeping person is to a certain extent an automaton, reacting as stimulated; judgment and discrimination are in abeyance. A completely hypnotised person is, in the fullest sense of the word, an automaton, reacting as stimulated by the operator; the stimulation or '*suggestion*' arouses in the brain of the subject an '*idea*' with crude and startling distinctness, unmodified by any scepticism or criticism, and produces with fatal certainty action appropriate to idea. A hypnotised patient believes everything his temporary 'master' tells him, and carries out every order he receives, moving in obedience to suggested ideas or provoked hallucinations. These have only a subjective existence, as is recognisable by the fact that the apparent object is not modified in appearance by optical instruments: *e.g.* an imaginary blot on a card is not doubled by a prism (unless indeed there should be real marks visible and doubled); a disc imagined as half red, half blue, is not seen purple when rotated. We recognise in the provoked hallucinations of a hypnotised subject an exaggeration of what normally occurs in a more or less marked degree in everyday life, not merely in the reflex reactions of the medullary axis, but in those of conscious imagination aroused by real objects. The ideas of things in the mind of the most exact observer, are no faithful copy of things in themselves, and in the consciousness of a careless observer depart in most extravagant ways from the actualities as they appear to a majority of normal men; in an insane person, or in a hypnotised person, the idea and the thing diverge to such an extent that the former becomes characterised as a hallucination or a delusion.

A child is 'impulsive,' reacts upon the suggestions of the moment—in a word, is more automaton-like than a reflective, self-controlled adult. Religious ecstasy, lovers' imagination, ordinary dream chains, somnambulism, the deceptions produced by the distracting manœuvres of a juggler, are more or less familiar instances of that concentration or predominance of a train of ideas—to the effacement of other accessory or modifying ideas and sensations—which in extreme degree is characteristic of the hypnotic state. Education is not only instruction, it is suggestion working upon brains more or less predisposed to reception, more or less preoccupied by the effects of previous suggestions; and the influence of some persons upon the beliefs and conduct of others is an everyday instance of physiological hypnotism, the actual result depending upon two factors—upon the impressiveness of the operators, upon the susceptibility of the subjects. A hypnotised person is in a state of '*suggestibility*' or unsceptical credulity, which is a retrogression towards a primitive state, and an exaggeration of that working credulity of everyday life which enables us to acquiesce in and act upon simple statements without constantly exacting argument or evidence or proof. We naturally—in the absence of stronger reason to the contrary—believe what we are told, and imitate the actions of other people. Suggestions to ideas and to actions have more or less pronounced effects on persons of different temperament; they have an exaggerated or forced effect upon hypnotised subjects during the passive state, or even, it may be, in their ordinary awakened condition. All men are more or less automata; hypnotised subjects are excessively or completely automata.

The influence of mind on body—using this expression in the ordinary undefined, yet sufficiently indicative sense—offers instances which, although not embraced by the term 'hypnosis,' bear however some relation to its phenomena, there being this point of similarity between them, that extra-ordinary body-effects are produced in both cases by concentrated mental attitudes. A person having swallowed a bread-pill in the belief that he has taken a purgative, will very possibly be purged; a person having received a hypodermic injection of water in the belief that morphia has been used, will very possibly go to sleep; railway-litigation-shock is mainly a disease by imagination, but none the less a very real disease. Far more surprising and to all appearance well-authenticated instances might be quoted (*e.g.* stigmata, faith-cures, &c.), but with marvels *quâ* marvels we are not concerned; the simple instances just given are quite sufficient to bring home to us the fact that 'state of mind' is a potent factor in state of body, and that the first aim of the physician should be to establish in his patient the idea of recovery.

Two great practical lessons are the immediate outcome of any intelligent study of hypnotic phenomena; the first is the lesson of self-distrust, the second is the lesson of self-confidence.

Every man's brain is more accessible to certain kinds of ideas than to certain other kinds; all men, even the most judicial, form opinions and convictions upon data selected by self-suggestion, coloured and refracted by their own mental media. We see and hear what we look or listen for, we believe what we wish for, and each man outside the province of his own tastes and sympathies, is in varying degree blind and deaf to actual phenomena; what he dislikes he disbelieves. A full and real apprehension that this is a necessary attribute of cerebral action cannot but be a corrective of that 'cocksureness' which is one of the blind alleys in which men's minds are apt to become blocked, and give practical value to the sentiment more often expressed than felt—'*You may be right, I may be wrong.*'

It is no less important—and for the physician it is immediately and specifically important—to fully realise the power of suggestion on men's minds and bodies. Like breeds like; self-distrust in the guide gives rise to want of confidence in the guided; self-confidence in the leader raises confidence in the follower. Nothing ensures success more than the confident expectation of success; the fear of failure often brings failure as its direct consequence. The physician who knows and trusts his own resources, will carry his patient through illness, where another man will vacillate and despond, and by his face or manner suggest failure and hasten death.

APPENDIX

I. ORIGIN AND NUTRITION OF THE EMBRYO

THE OVUM.	Maturation .	polar globules, female pronucleus.	germinal vesicle.
	Fertilisation .	spermatozoon, male pronucleus.	
	Segmentation.		
	Organisation .	The three primary layers, their fate and functions in the adult.	

Hypoblast .	The digestive tract.		The allantois and placenta.
Mesoblast .	The vascular system.	First or vitelline.	
„ .	Second or allantoic.	Vascular changes at birth.	The amnion.
Epiblast .	The nervous system.		

Experimental physiology of the embryo.—Composition of a fresh hen's egg, and of a newly hatched chick. Respiration within the egg. Origin of hæmoglobin.

Respiration of the mammalian embryo. Blood-gas analyses. Blood-pressure and blood-flow in the umbilical vessels. Hæmoglobin. Heat-production. The renal function; indigo-carmine experiments. The digestive ferments. The hepatic function; meconium. Glycogenesis. Structure and properties of the chick's heart *in ovo*.

WE do not undertake to give even a summary description of the anatomical development of particular parts, organs, and tissues. However essential such descriptions may be to the comprehension of adult malformations of medical as well as of surgical interest, we regard them as being outside physiological bounds, and to be learned far more thoroughly and easily in their appropriate place. Nor shall we enter upon any description of the mechanism of coitus or of the phenomena of menstruation and parturition; we may, indeed, point to the former as a well-marked example of spinal reflex discharge in consequence of summated stimuli (p. 484), and we may mention the fact that parturition itself can be effected as a reflex act from the lumbar portion of the cord separated from the brain by transverse division; but the detailed description of parturition and of menstruation belongs properly to the province of obstetrics; the only points which may perhaps be mentioned here as being of physiological interest are, that each menstrual flux is probably accompanied by the discharge of an ovum, that the most frequent seat of fecundation of ovum by spermatozoon is probably the upper part of a fallopian tube, and that according to the somewhat limited range of trustworthy statistics available, impregnation appears to have occurred most frequently during the first week after a menstrual period.

There are, however, several organs the functions of which are accessible to study in embryonic life, and general ideas relating to nutritive functions illustrated in the development of the embryo, as well as various anatomical questions immediately bearing upon physiological doctrine, which demand attention from a physiological standpoint. These we shall consider, and in so doing shall find it necessary to recognise where we are, and how certain embryonic conditions have been reached.

The entire human body is originally derived from a single female cell, the *ovum* or germ-cell, modified by the action of a male cell, the *spermatozoon*. The process of fertilisation consists in the conjugation of these two cells or of portions of them, and is preceded by certain preparatory changes occurring in the ovum prior to the advent of the spermatozoon, collectively termed *maturation*, viz. an extrusion of part of its nucleus in the form of the first and second 'polar globules,' the remainder of the nucleus being termed the 'female pro-nucleus.' Maturation of the ovum having been accomplished, *fertilisation* proper commences by penetration of a spermatozoon; the head of the spermatozoon enlarges, forms the 'male pro-nucleus,' and fuses with the female pronucleus, forming a new nucleus, the true germinal vesicle; the nucleated cell is now fertilised and capable of undergoing cell-multiplication by cell-division and cell-growth. The next stage is *segmentation*. The single cell, with its nucleus formed from male and female pronuclei, divides into two cells, each of these into two, and so on, giving rise to a growing mass of multiplying cells, 2, 4, 8, 16, 32, 64, &c. In mammals the entire mass of the cell is involved in this process; in birds it is confined to a small portion of the much larger mass which forms the yolk of an egg.

We may at this point attend to the differences of structure, development, and nutrition between the two classes of ova, the fate of which most concerns or instructs us, *i.e.* that of a bird, and that of a mammal. A hen's egg comprises the ovum proper or yolk, and accessory envelopes of albumen and of mineral matter; if it be a fertilised egg, it will after twenty-one days' incubation contain a bird which has replaced the originally white and yellow materials. These materials were in chief part the food-store at the expense of which an originally minute portion of protoplasm has grown, multiplied, and developed. A human ovum is a small cell ($\frac{1}{5}$ mm in diameter), comprising little more than its own protoplasm; its yolk is in very scanty amount, it has no surrounding albuminous provision. The whole cell divides and subdivides if fertilised, and not having in itself any considerable store of food, its nourishment and augmentation depend upon the mother organism, at first by simple imbibition, later by nutritive and excretory osmosis through a special organ—the placenta—which is its respiratory and alimentary and excretory organ.

The first step in the development of the mammalian ovum is cell-multiplication; the first step in organisation is the regular arrangement of its now numerous cells as a vesicle, the blastodermic vesicle, with an accumulation of small granular cells at one pole—the future blastoderm. The first step in differentiation is the distinction visible between upper or outer and lower or inner ranks of cells at this spot, soon followed by an obvious triple division into upper or epiblastic, lower or hypoblastic, and middle or mesoblastic layers. This tripartite distinction is fundamental, the different tissues and organs in adult life are traceable back to these three stocks respectively, and already in the three ancestral membranes we may recognise in the germ a differentiation of function which is preserved throughout life. The upper or external layer is neural; it will form epithelium—the general epithelium of the skin, the special epithelium of sense-organs, and by involution, the central axis of the cerebrum and spinal cord. The lower or internal layer, lying on the yolk, is nutritive; it will form the digestive and absorbent epithelium of the intestine and intestinal glands. The middle layer is the massive working layer, the future bone and muscle of the body, and at a very early stage it shows tokens of the depuratory and excretory functions which are among its functions in after life; it is the nidus of origin of the entire vascular system and of the blood, and one of the earliest organs to appear in it is the Wolffian body, which forms in the adult the essential parts of the renal and generative organs—of the kidney, testicle, and ovary.

The dorsal or epiblastic surface of the blastoderm rises in two longitudinal ridges which, coming together and coalescing in the middle line, form the medullary tube or axis. The anterior, posterior, and lateral margins of the blastoderm turn downwards and converge, enclosing a cavity, the visceral tube, between which and the yolk vesicle a communication long remains as the vitelline duct. In the bird's egg, towards the middle of incubation the vesicle contains the true yolk surrounded by blastoderm; in the mammal, the 'yolk-vesicle' contains much more than the original yolk: it is of new formation, and consists of all that part of the blastodermic vesicle which is not directly involved by the forming embryo, and is termed the umbilical vesicle.

The ventral or hypoblastic surface, in consequence of the folding downwards of the entire blastoderm, soon forms a widely open ditch terminating in two cæca—foregut and hindgut—which at a later intrusion of the stomodœum and proctodœum, become œsophagus and rectum. The intermediate portion becoming tubular, lengthens and curls up, dilates in some parts, and pushes out processes at others, forming finally the rest of the intestinal canal and its accessory digestive glands (liver, pancreas). A protrusion from the hindgut forms the allantois, the dilated stalk of which persists in after life as the urinary bladder. The anterior portion or foregut likewise buds forth processes, some of which form temporary communication with the exterior, as the pharyngeal clefts, while others ultimately give rise to permanent glands (thymus, thyroid), which become ductless by obliteration of their original stalks, and others finally form the salivary glands and the most important of adult nutritive and excretory organs—the lungs. The only so-called 'glands' which do not originally spring from the

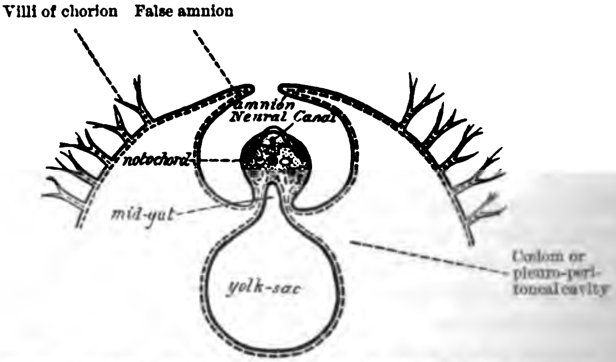


FIG. 289.—DIAGRAMMATIC TRANSVERSE SECTION OF EMBRYO AND OF ITS ANNEXES. The mesoblast is indicated by the broken line. (Quain's Anatomy.)

hypoblast are the supra-renals, which are developed in association with the sympathetic system from mesoblastic and probably also from epiblastic tissue; and the spleen, which is an appendage of the vascular system.

With regard to the middle or mesoblastic layer, the most important points to be understood, in addition to those mentioned above, are, its relations to the fœtal membranes, and to the two layers above and below it. Its lateral plates as distinguished from the axial mass are themselves distinguishable as somatic and splanchnic; the former or upper layer conjoined with the epiblast, forms the body wall and the dorsal membrane or amnion, which surrounds and encloses the embryo, as will presently be described; the latter or lower layer conjoined with the hypoblast, forms the visceral wall and the secondary ventral vesicle or allantois, which will form the temporary organ by which the fœtus is nourished—the placenta.

Early in the existence of the embryo, folds arise around it, formed from the dorsal or somatic layer, which finally coalesce dorsally and form an enclosing membrane, the *amnion*. Of the double layer by which the enclosure is effected, the outer or false amnion fuses with the general covering or chorion; the inner or true amnion alone remains as a distinct membrane; ultimately the embryo floats free in its cavity, which is filled with fluid; its only attachment to the mother is by the umbilical cord, which, as we are about to describe, is formed by the allantois. The main use of the amniotic fluid is mechanical, affording protection to mother and child from sudden movements of either; it is a dilute fluid, with albumen and only a trace of urea; at term it amounts to between 500 and 1,000 c.c. It cannot be regarded as a nourishment fluid, or an excretion fluid; the embryo gets proteid and gets rid of urea by way of the placenta.

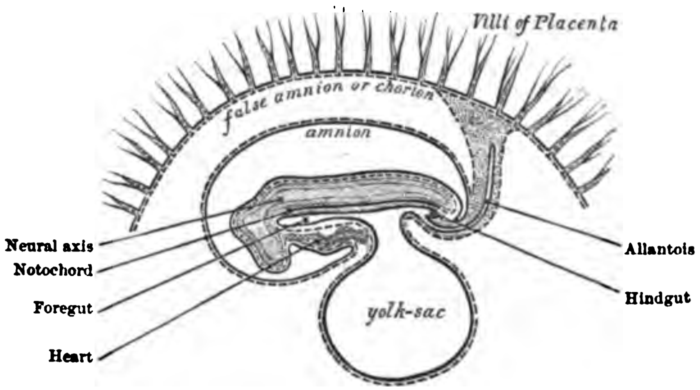


FIG. 290.—DIAGRAMMATIC LONGITUDINAL SECTION OF EMBRYO AND OF ITS ANNEXES.
The mesoblast is indicated by the broken line. (Quain's Anatomy.)

A more important structure, physiologically, is the *allantois*; budding forth from the hindgut, it insinuates itself between the two layers of the amnion and coalesces with the outer layer. It is pre-eminently a vascular organ; the ramifications of the allantoic vessels occupy the embryonic villi, which after an early stage as a uniform shaggy covering, ultimately dwindle at parts and enormously increase at one spot in correlation with increase of the uterine lining. The *placenta* is thus established as the temporary organ through the medium of which everything needed by the growing embryo is obtained from the mother, and everything produced by its metabolism discharged. The organ must therefore transmit proteid, fat, carbohydrate, water, salts, and oxygen from maternal to fœtal blood—carbon dioxide and urea from fœtal to maternal blood.

The embryonic vascular systems.—The first circulation of blood established in connection with the embryo is that of the yolk sac by the *vitelline* arteries and veins; the ramifications form the *area vasculosa*, resting on the surface of the yolk; it is the vehicle by which food is conveyed from yolk to embryo. The vitelline circulation is a temporary one, forming, increasing, and then dwindling away with the gradual consumption of the yolk, and subsequently replaced by the allantoic circulation; in the bird's egg it is comparatively far more prominent than in the mammalian ovum, in which the chief nutrition is from the mother by way of the placenta.

The second circulation of blood is established by the allantois, which arises from the hindgut as just described, and increases as the yolk-sac decreases; its pedicle of origin becomes the umbilical cord, its vessels the umbilical arteries and veins. Vessels within the embryo, connected with these two extra-embryonic systems, form and alter in correspondence with their alterations. The heart appears first as a double tube, then as a single sac, which pulsates rhythmically before nerves, or even muscle, or blood-corpuscles have made their appearance. The vitelline blood comes to the embryo from the '*area vasculosa*' of the yolk-sac by the vitelline veins, and returns by the vitelline arteries. Later, when the vitelline has made way for the allantoic system, blood comes from the placenta by the umbilical vein in the arterialised state to the embryo, and returns to the placenta in the venous state by the umbilical arteries. Now—that is, when the placental function is fully established, the embryonic vascular system exhibits features of structure in obvious correspondence with physiological conditions. The umbilical vein, bringing oxygenated and otherwise renovated blood, enters the liver, some passing straight on by the ductus arteriosus to the inferior cava, the rest after a portal ramification in the liver. The mixed blood in the cava is sent through the right into the left auricle, being guided through the foramen ovale by the eustachian valve. From the left auricle it passes to left ventricle and to aorta, thus in main part to the cephalic end of the body, whence it returns by the superior cava to the right auricle, through which it is guided by the eustachian valve into the right ventricle. From the right ventricle it is sent through the pulmonary trunk, ductus arteriosus, and thoracic aorta, in main part to the placenta by the umbilical arteries, in small part to the caudal end of the body.

Thus in the fœtal circulation we have to distinguish at least four qualities of blood—(1) the purest blood, returning from the placenta, and for the most part passing through the liver; (2) the least pure blood, returning from the inferior extremities; (3) the mixture of these two kinds, passing to the left ventricle and cephalic end; (4) the returning cephalic blood, passing to the caudal end and to the placenta.

The noteworthy features from a physiological standpoint, briefly enumerated, are: (1) the smaller difference between typical venous and typical arterial blood in the fœtus than in the adult; (2) the great size and importance of the liver, which exercises its action upon almost the entire mass of the incoming blood—an action which has its most obvious tokens in the comparatively large amount of oxygen lost by that blood in its transit through the liver, and in the large accumulation of biliary excreta in the meconium formed during fœtal life; (3) the fact that whereas the head end of the fœtus receives mainly new blood, the tail end receives only second-hand blood; it will therefore not be matter for surprise that at term the head is far more bulky than the inferior extremities in comparison with their relative bulk in after life;

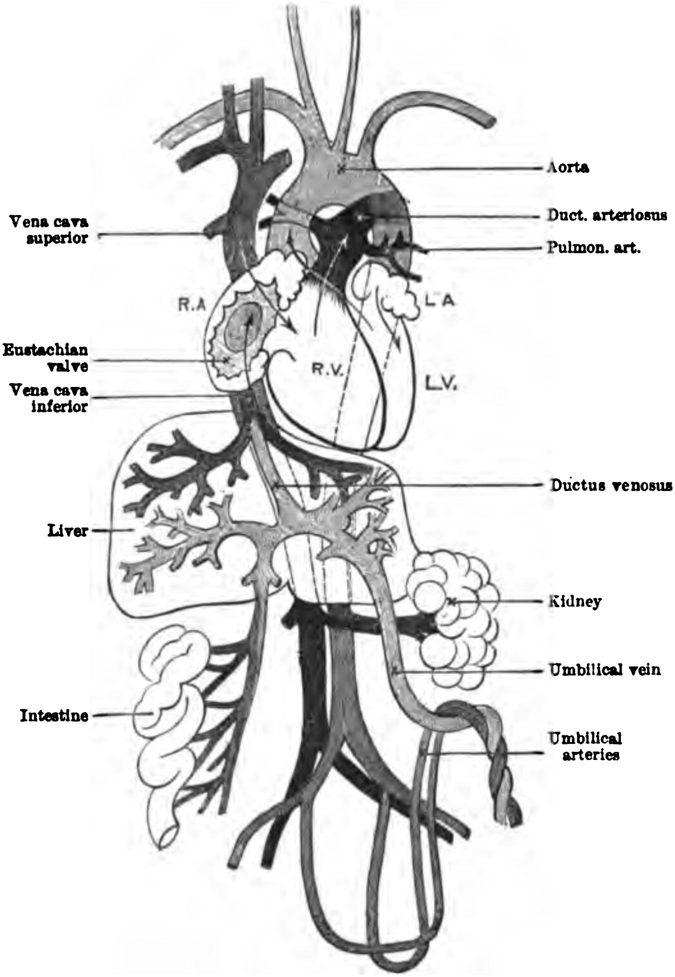


FIG. 291.—THE FŒTAL CIRCULATION. (Quain's Anatomy.)

(4) the equal thickness of the right and left ventricles of the fœtal heart in contrast with their inequality in the adult organ; the equality and inequality being in obvious correlation with the equality and inequality of resistance to be overcome by the two ventricles in the two states respectively. During the first few days of independent life, in consequence of its separation from the placenta and of the expansion of the pulmonary circulation, the circulatory currents are completely altered; the umbilical blood-flow ceases, and the vessels close, the ductus venosus ceases to be pervious, the pulmonary vessels expand, the ductus arteriosus shrinks and becomes impervious; finally, the foramen ovale between the two auricles becomes more and more completely sealed by the adhesion of its valvular membrane to the margin of the orifice. The cardiac chambers and blood-flow are now in their well-known adult form.

Origin of the nervous system.—A knowledge of the developmental history of the nervous system is of some assistance to the due comprehension of its functional significance, and we shall therefore allude to one or two leading facts, and give a tabular summary to show the genealogy of the main masses in the adult brain. Originally the whole cerebro-spinal and sympathetic system is of epidermic or epiblastic source.[1] The outer or upper layer of the embryo grows in and becomes embayed and cut off by the medullary folds to form an axial dorsal tube. The anterior part of the tube becomes dilated; the dilatation, being incompletely chambered by transverse constrictions, forms the three primary cerebral vesicles, fore-brain, mid-brain and hind-brain. The fore-brain pushes out a lateral pair of hollow processes, which form the optic vesicles and become the retina and optic nerves, and an anterior pair of vesicles which become the hemispheres of the cerebrum. The nerves, cranial, spinal, and sympathetic, arise as outgrowths budding forth from the medullary grey axis and extending with the progressive extension of the periphery. The correspondence between parts of the embryonic brain and parts of the adult brain is as follows:

I. *Fore-brain*=3rd ventricle and optic thalamus.
its lateral vesicles=optic nerves and retinæ.
its anterior vesicle=hemispheres and corpora striata; olfactory lobes.
II. *Mid-brain*=iter a tertio ad quartum ventriculum, corpora quadrigemina and crura cerebri.
III. *Hind-brain*=4th ventricle, cerebellum, pons, spinal bulb.

The internal surface lined by ciliated epithelium is recognisable in the adult as the central canal of the cord and ventricles of the brain.

---

[1] The epiblastic origin of cranial and spinal nerves is unquestionable; that of the sympathetic system is more doubtful, and although its origin as an outgrowth is very generally accepted, recent observations are to the effect that the sympathetic arises independently as a lateral rod of mesoblast from which processes grow inwards, and thus establish connection with the medullary axis. (Paterson.)

The surrounding grey matter forms the central or medullary grey matter of the bulb and cord.

The most striking features from a physiological standpoint are, (1) that the medullary grey axis forming the grey matter of the spinal bulb and cord, is the original stem from which nerves take their source and the higher centres expand; (2) the excessive development of the cerebral hemispheres, which in man grow above and overshadow, physiologically as well as anatomically, the bulbar end of the medullary axis, and cause it to occupy a comparatively unobtrusive position, under cover as well as under control.

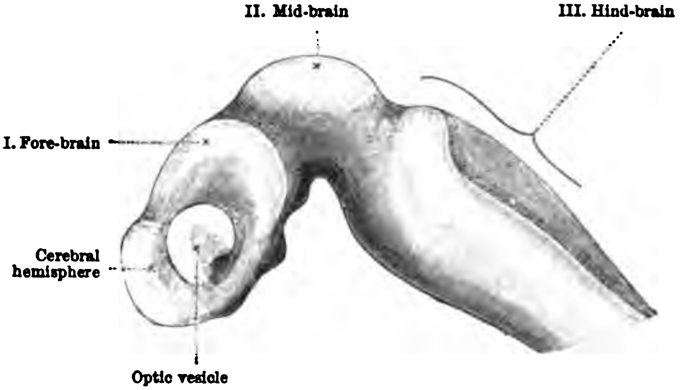


Fig. 292.—The Fœtal Brain. (Quain's Anatomy after His.)

The special sense organs are of epiblastic source. Tactile organs are and remain superficial. Auditory and olfactory organs arise by recession and burrowing of the superficial epiblast; the nose remains freely open, the internal ear is cut off and enclosed by secondary mesoblastic development. The visual organ, on the other hand, although in its essential parts epiblastic, is completed in structure by mesoblastic contributions; the most essential part of the organ—the retina, arises as a hollow process from the fore-brain, itself of epiblastic origin; while the lens is produced by inward recession of the epiblast, and received by the optic vesicle, which becomes folded round the ingrowing mass as a double layer, which, however, leaves a gap at its inferior margin. This gap, but for which the lens and vesicle might be correctly represented as head and double-layered night-cap, is the choroidal fissure through which mesoblastic tissue subsequently reaches the interior of the eyeball, and forms its internal vascular and connective tissue constituents—vitreous body, arteria centralis, iris and ciliary muscle; the external vascular and fibrous coats—sclerotic, choroid, cornea are formed from the surrounding mesoblast.

The development of nerve tracts has already been considered in some detail in connection with the spinal cord and with the regeneration of divided nerves; to the sequence—pale fibre, fine medullated fibre, coarse medullated fibre—we may add the still earlier stage of *neuroblast*, which is described by His as the earliest state of nerve-cell and dependent nerve-fibre, as distinguished from the *spongioblast*, which is the origin of the neuroglia cell and network, forming the supporting tissue of grey matter.

Experimental Physiology of the Embryo

From the physiological anatomy of the embryo, many general principles regarding its nutrition may legitimately be inferred; we now propose to briefly review the chief points actually verified by observation and experiment, confirming and amplifying such inferences.

Chemical composition of hen's egg at beginning and end of incubation.—A fresh egg has the following composition:—

Shell 5			
White 30	Proteids, albumen and globulin . . .	3	
	Fats, &c.	0·3	
	Salts	0·1	
	Water	26·6	Solids 9·4
Yolk 15	Proteids	1·7	Water 35·6
	Fats	3	Total 45 grm
	Lecithin	1	
	Vitellin, nuclein, glycogen . . .	0·2	
	Salts	0·1	
	Water	9	

The provision in the fresh egg is nearly 5 grms. proteid and over 3 grms. fat; of carbohydrate only traces, it being formed (? from proteid) in the course of incubation. During the twenty-one days' incubation the shell undergoes no change; the embryo gets salts from the contents of the egg and not from its shell. The contents of the egg weighing 45 grms., the embryo chick formed therefrom will weigh about 10 grms. less; the loss consists of water, of carbon dioxide (·5 grm.), and, according to Liebermann, of an undetermined quantity of nitrogen. The new-hatched chick, weighing 35 grms., consists of about 7 grms. of solids and 28 grms. of water.

A fresh egg of normal weight (50 grms.) contains about 5 grms. shell, 30 grms. white, 15 grms. yellow. The total solids in the contents amount to 10 grms.; at the end of incubation they have diminished by $\frac{1}{4}$, *i.e.* during incubation carbon has been given off as CO_2, and—according to comparison between the total nitrogen in the fresh egg and in the new hatched chick—nitrogen has also been given off. There is no difference appreciable between the salts of a fresh egg (without shell) and of a newly hatched embryo, *i.e.* the shell does not contribute to the formation of the chick. As regards water, the early embryo contains it in larger proportion than the contents of the egg or than the formed chick, *e.g.* 90 per cent. in the former as compared with 80 per cent. in the latter two; although during the period of incubation water has been lost from the egg. Fat (in the yolk) forms fatty acid during incubation. The proportion of hæmoglobin is at first very small; at half time only $\frac{1}{700}$, at full time $\frac{1}{200}$, in the adult hen $\frac{1}{140}$ (Liebermann). The important point to recognise is that death of tissue is associated with the very beginning of the life of tissue. Katabolic effects are manifested at the very outset in association with anabolic phenomena. But not only does a fertilised egg exhibit respiratory phenomena by yielding CO_2; an unfertilised egg likewise does so; this is token that such an egg is also composed of living matter, although that matter is incapable of spinning the complete cycle. On reference to the table at p. 129 it may be noticed that the respiratory activity of the chick embryo has about the same value as that of a hibernating animal: if the shell, which is the porous septum through which the exchange of gases is effected, be varnished, the inhabitant will perish by asphyxia.

Respiratory activity of mammalian fœtus. Blood-gas analysis.—The most obvious of the functions of the placenta is respiratory; blood passing from mother to child by the umbilical vein is of brighter colour than blood passing from child to mother by the umbilical arteries. And further insight has been obtained into the process by the gas-analysis of the blood of sheep embryos, which at full term weigh about as much as human embryos. The following values were obtained by Zuntz and Cohnstein:—

		CO_2	O_2	
Lamb at full term weighing 3·6 kg.	umbilical artery .	47	2·3	vols. per 100
„ „	umbilical vein .	40·5	6·3	„

the rate of blood-flow was about 44 cc. per minute, *i.e.* carrying 1·76 cc. O_2 and 2·86 cc. CO_2, *i.e.* the respiratory activity of the fœtus was less than $\frac{1}{10}$ that of a normal adult sheep.

The *blood-pressure* in the same instance was between 6 and 8 cm. Hg. in the artery, and half that value in the vein, thus illustrating the fact that the difference between arterial and venous blood-pressure is much greater in the adult than in the fœtus. The fœtal pulse can be felt in the umbilical cord for a short time after delivery, but with the closing up of the umbilical artery, it vanishes. The first respiration of a new-born infant occurs in response to the combined effect upon the spinal bulb of the increasing venosity of the blood following the arrest of the placental respiration, and of cutaneous stimuli by cold air, or it may be by the flip of a wet towel.

An important peculiarity exhibited by fœtal blood, and referable to the fact that such blood contains an abundance of active cellular elements (nucleated red corpuscles) is the much greater rapidity of respiratory changes occurring in the blood itself; in a given volume of fœtal blood a larger quantity of O_2 is consumed and of CO_2 is produced than in an equal quantity of adult blood. Also in relation to fœtal respiration it should be mentioned that the amount of hæmoglobin in the body is at first much below that of the adult, and that it gradually approximates to it in the course of pregnancy; at half time the relation of hæmoglobin to body-weight is only $\frac{1}{700}$, at full time $\frac{1}{200}$, in the adult $\frac{1}{140}$ (egg and hen); in an early sheep-fœtus the hæmoglobin value may be only $\frac{1}{10}$th that of the adult; at term it amounts to . From which we learn that the respiratory function develops slowly. At birth it undergoes a sudden change—in the sheep it is increased tenfold; from which we learn further that the conditions of active respiration are already present at a time when for want of excitant the process itself is still smouldering at low intensity.

In relation to the same process there is another point which is of considerable practical importance. In normal parturition, the birth of the child precedes that of the placenta, and after a shorter or longer interval the cord is ligatured and divided; it makes a great difference to the child whether this be done immediately or some time after birth; in the latter case uterine pressure squeezes blood from placenta to child and on the average the difference so effected is from 50 to 100 cc. A normal child of 3 kg. should have 300 cc. of blood, a child after immediate ligature may have as little as 200 cc. The fact has been verified on the human subject, a child placed on a balance shortly after delivery and left connected with the placenta in utero gradually increases in weight by about 50 grammes.

The tissues of an embryo produce far less heat than those of the adult; there is no such thing as thermotaxis during embryo-life, the temperature of a fœtus is only one or two tenths of a degree above that of the mother; the heat of the embryo is carried off by the uterine circulation precisely as heat produced by the liver is carried off by the hepatic circulation; this low production of heat is in correspondence with the low respiratory activity and with the tenacity of life exhibited by an embryo deprived of oxygen; an embryo is slowly asphyxiated in utero if the placental circulation is arrested, it is rapidly asphyxiated by asphyxia of the mother with intact placental circulation; in the former case embryonic tissue slowly consumes the oxygen it possesses, in the latter case, the maternal tissue rapidly consumes oxygen and withdraws it from the fœtus.

It is probable that the nitrogen metabolism is also of much lower intensity in the fœtus than in the adult; to the question as to its mode of elimination by a fœtus in utero, it may be answered that although towards the end of the pregnancy the kidneys are evidently beginning to act, it is probable that the placenta is the main organ of urinary excretion during the period of pregnancy. The bladder of a newborn fœtus is sometimes empty, sometimes full, the amniotic fluid contains only a small proportion of urea, cases are on record of a fœtus born at full term and possessing no kidneys; these are the main facts upon which the answer is based.

The entire nutrition of the fœtus after an early period is in fact dependent upon the placenta; the amniotic fluid, to which nutritive action has been attributed, may indeed slightly contribute in this direction, but in very minor degree; it contains very little albumin and no carbo-hydrate or fat; whereas the placenta is a highly glycogenic organ, and has also been asserted to contain peptone.

That the amniotic fluid is of maternal rather than of fœtal origin is clearly shown by Zuntz's experiments; after injection of indigo-carmine into the vessels of a pregnant sheep he found the placenta and amniotic fluid coloured blue, without extension of colour to the fœtus itself, or even after destruction of the fœtus. On the other hand, after direct injection of carmine into the fœtus he found its kidneys blued, which was proof that the organs even if not ordinarily in action, yet are evidently capable of excretory activity.

With regard to the existence and digestive activity of embryonic ferments—ptyalin, pepsin, pancreatin—artificial digestion experiments have furnished no very precise results, either positive or negative; or, rather, both positive and negative results have been reported by different observers. There can be no doubt that the digestive action of fœtal glands is at any rate much less constant and pronounced than that of adult glands, but it is probable that the ferments do already exist in the fœtal organs in their zymogen state.

By far the most important of fœtal organs is the liver; beginning at about mid-pregnancy, or even sooner, the excretion of bile and its accumulation in the meconium are unmistakable tokens that important chemical events are taking place in the liver; so also is the fact alluded to above that the liver is the chief seat of the oxygen consumption by the fœtus.

The chick's heart from the fourth day of incubation onwards is capable of being submitted to certain observations and experiments; the contraction, which is at first at very irregular intervals, sweeps over the tube in a peristaltic manner from the venous to the arterial end, and by means of photography its rate of progress has been determined to be 5 to 10 mm. per sec. (Fano). Placed in a watch-glass in a few drops of fluid it forms an exceedingly sensitive reagent to the action of drugs, and to that of nutrient or non-nutrient fluids; muscarin stops it; the beats die out in salt solution, and may be renewed by serum-albumin; examined in a gas chamber the beats rapidly disappear with carbon dioxide and reappear under the influence of oxygen; and attention may be drawn to the fact that there is here no possible complication by action on nerve-fibres or on ganglion-cells, which do not yet exist. Submitted to tetanising currents, the embryonic, unlike the adult heart, is completely tetanised.

According to Hermann and v. Gendre the developing chick's embryo may exhibit an E.M.F. of $\frac{1}{100}$ Dan., any part of the dorsal surface of the embryo being positive to any point of the yolk; thus in the embryo itself the current is directed from ventral to dorsal surface.

II. CONSTITUTIONAL FORMULÆ OF SOME OF THE CHIEF PROXIMATE PRINCIPLES

The chemical relations of several of the more important substances mentioned in Chapters V. and VI., such as the fats and many of the nitrogen compounds, will be better appreciated by considering their constitutional or linkage formulæ, and the position which these formulæ occupy in well-known series. This point of view is particularly serviceable in the case of *urea*, *glycin*, *sarcosin*, *taurin*, *leucin*, and *tyrosin*, the constitutional formulæ of which can be given on a satisfactory basis; but it is not without value in the case of other complicated substances represented in a more or less hypothetical form, such as *uric acid*, *hippuric acid*, *creatin*, *creatinin*, *indican* (so-called), *indol*, *skatol*, *cholesterin*, *lecithin*, *cystin*. The fats can be usefully so represented; the carbohydrates, however, with perhaps the exception of *dextrose*, cannot be so treated for want of sufficient knowledge: we have no idea how to represent a molecule of *starch* or of *glycogen*, or of *dextrin*. As for the proteid group, and substances such as hæmoglobin, bile-pigments, &c., their graphic formulæ must be recognised as imaginary pictures containing radicles grouped so as to show possibilities, and arranged to suit a very scanty knowledge of facts.

The elements we have to deal with are hydrogen, oxygen, nitrogen, carbon, and occasionally phosphorus and sulphur.

The chief radicles entering into the composition of bodies which we have to consider, are: hydroxyl, HO; amidogen, NH_2; the hydrocarbon radicles CH_3, C_2H_5, C_3H_7, C_3H_5, &c.; and the benzene radicles C_6H_5, C_6H_4, &c.

We shall best form an idea of their combinations by considering—

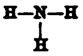
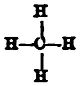
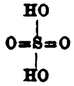
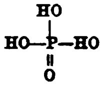
(1) Some simple linkage-formulæ of familiar bodies, H_2O, NH_3, CO_2, HNO_3, H_2SO_4, H_3PO_4.

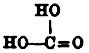
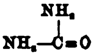
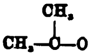
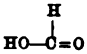
(2) The linkage-formulæ of a simple fatty acid series, of the combination of some of its members with the glycerine radicle C_3H_5 as *fat*, and of two or three organic compounds with nitrogen, which from the chemical point of view fall into place on the lines of series running parallel with a simple fatty acid series.

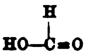
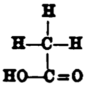
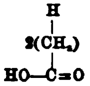
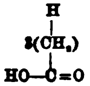
(3) Linkage-formulæ which include a benzene nucleus C_6H_5.

(4) Linkage-formulæ of a complicated or not definitely settled type.

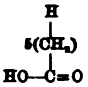
The ordinary or empirical formulæ of water, ammonia, &c., translated into linked formulæ are as follows—

Water	H_2O	H—O—H
Ammonia	NH_3	 $H\text{—}\underset{\underset{H}{\mid}}{N}\text{—}H$
Marsh gas	CH_4	 $H\text{—}\overset{\overset{H}{\mid}}{\underset{\underset{H}{\mid}}{C}}\text{—}H$
Carbon dioxide	CO_2	O=C=O
Sulphuric acid	H_2SO_4	 $O\text{=}\overset{\overset{HO}{\mid}}{\underset{\underset{HO}{\mid}}{S}}\text{=}O$
Phosphoric acid	H_3PO_4	 $HO\text{—}\overset{\overset{HO}{\mid}}{\underset{\underset{O}{\parallel}}{P}}\text{—}HO$

The formula of the hypothetical compound carbonic acid, H_2CO_3—which, although not known as a free compound, but only as H_2O+CO_2, is indicated as a rational combination by the existence of corresponding salts Na_2CO_3, K_2CO_3, &c.—serves as the starting-point of the series of fatty acids and the type upon which urea is constructed. Its linked formula is  $HO\text{—}\overset{\overset{HO}{\mid}}{C}\text{=}O$; that of urea is  $NH_2\text{—}\overset{\overset{NH_2}{\mid}}{C}\text{=}O$; that of acetone is  $CH_3\text{—}\overset{\overset{CH_3}{\mid}}{C}\text{—}O$; and substituting H for one of the hydroxyl radicles HO we have  $HO\text{—}\overset{\overset{H}{\mid}}{C}\text{=}O$ or formic acid, which is the starting-point of the fatty acid series, $C_nH_{2n+1}.\ CO.OH$, where CH_2 or a multiple of CH_2 is the difference between different members of the series.

Formic acid.	CH_2O_2	or	 $HO\text{—}\overset{\overset{H}{\mid}}{C}\text{=}O$	or	H. CO.OH
Acetic acid.	$C_2H_4O_2$	or	 $H\text{—}\overset{\overset{H}{\mid}}{\underset{\underset{HO\text{—}C\text{=}O}{\mid}}{C}}\text{—}H$	or	$CH_3.\ CO.OH$
Propionic acid.	$C_3H_6O_2$	or	 $\overset{\overset{H}{\mid}}{\underset{\underset{HO\text{—}C\text{=}O}{\mid}}{2(CH_2)}}$	or	$C_2H_5.\ CO.OH$
Butyric acid.	$C_4H_8O_2$	or	 $\overset{\overset{H}{\mid}}{\underset{\underset{HO\text{—}C\text{=}O}{\mid}}{3(CH_2)}}$	or	$C_3H_7.\ CO.OH$

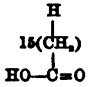
Caproic acid. $C_6H_{12}O_2$ or



$$\begin{array}{c} H \\ | \\ 5(CH_2) \\ | \\ HO—C=O \end{array}$$

or $C_5H_{11}.\ CO.OH$

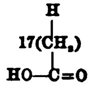
Palmitic acid. $C_{16}H_{32}O_2$ or



$$\begin{array}{c} H \\ | \\ 15(CH_2) \\ | \\ HO—C=O \end{array}$$

or $C_{15}H_{31}.\ CO.OH$

Stearic acid. $C_{13}H_{36}O_2$ or



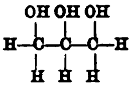
$$\begin{array}{c} H \\ | \\ 17(CH_2) \\ | \\ HO—C=O \end{array}$$

or $C_{17}H_{35}.\ CO.OH$

Fatty acids, fats, and soaps.—The animal fats are combinations of palmitic, stearic, and oleic acids with glycerin, in the form of tripalmitates, tristearates, and trioleates of glycerin.

Glycerin is a triacid alcohol having the empirical formula $C_3H_8O_3$, the constitutional formula $C_3H_5(OH)_3$

or



$$\begin{array}{ccccccc} & & OH & OH & OH & & \\ & & | & | & | & & \\ H & — & C—&C—&C & — & H \\ & & | & | & | & & \\ & & H & H & H & & \end{array}$$

Palmitate of glycerin or *tripalmitin* is constituted as follows—

$$C_3H_5\begin{cases} OH \\ OH \\ OH \end{cases} + \begin{matrix} C_{15}H_{31}COOH \\ C_{15}H_{31}COOH \\ C_{15}H_{31}COOH \end{matrix} = C_3H_5\begin{cases} C_{15}H_{30}COOH \\ C_{15}H_{30}COOH \\ C_{15}H_{30}COOH \end{cases} + \begin{matrix} H_2O \\ H_2O \\ H_2O \end{matrix}$$

Glycerin + *Palmitic acid* = *Tripalmitin* + *Water*

Stearate of glycerin or *tristearin* is constituted as follows—

$$C_3H_5\begin{cases} OH \\ OH \\ OH \end{cases} + \begin{matrix} C_{17}H_{35}COOH \\ C_{17}H_{35}COOH \\ C_{17}H_{35}COOH \end{matrix} = C_3H_5\begin{cases} C_{17}H_{34}COOH \\ C_{17}H_{34}COOH \\ C_{17}H_{34}COOH \end{cases} + \begin{matrix} H_2O \\ H_2O \\ H_2O \end{matrix}$$

Glycerin + *Stearic acid* = *Tristearin* + *Water*

Oleate of glycerin or triolein is constituted as follows—

$$C_3H_5\begin{cases} OH \\ OH \\ OH \end{cases} + \begin{matrix} C_{18}H_{34}O_2 \\ C_{18}H_{34}O_2 \\ C_{18}H_{34}O_2 \end{matrix} = C_3H_5\begin{cases} C_{18}H_{33}O_2 \\ C_{18}H_{33}O_2 \\ C_{18}H_{33}O_2 \end{cases} + \begin{matrix} H_2O \\ H_2O \\ H_2O \end{matrix}$$

Glycerin + Oleic acid = Triolein + Water

Animal fat is a mixture of these three glycerides—tripalmitin, tristearin, and triolein.

Fatty acids and fats are saponified by treatment with an alkali; soaps are compounds of the fatty acids with sodium or potassium, viz. palmitate, stearate and oleate of sodium or potassium.

$$C_{16}H_{32}O_2 + KOH = C_{16}H_{31}O_2K + H_2O$$

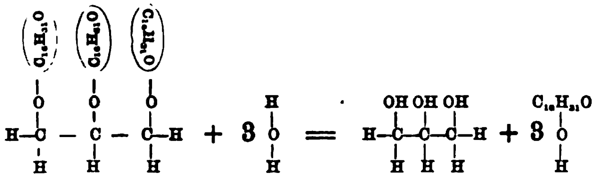
Palmitic acid + Potash = Potassium palmitate + Water

$$C_3H_5\begin{cases} C_{16}H_{32}O_2 \\ C_{16}H_{32}O_2 \\ C_{16}H_{32}O_2 \end{cases} + \begin{matrix} KOH \\ KOH \\ KOH \end{matrix} = \begin{matrix} C_{16}H_{31}O_2K \\ C_{16}H_{31}O_2K \\ C_{16}H_{31}O_2K \end{matrix} + C_3H_5\begin{cases} OH \\ OH \\ OH \end{cases}$$

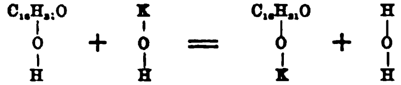
Tripalmitin + Potash = Potassium palmitate + Glycerin

Stearic and oleic acids, tristearin and triolein undergo similar transformation on treatment with an alkali.

These relations may be graphically represented as follows—



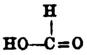
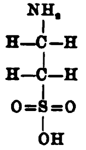
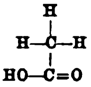
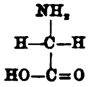
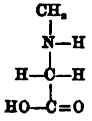
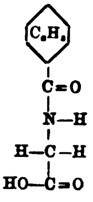
Tripalmitin + Water = Glycerin + Palmitic acid



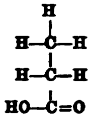
Palmitic acid + Potash = Potassium palmitate + Water

The analogous stearic and oleic compounds can be represented in a similar form, the palmitic radicle ($C_{16}H_{31}O$) being replaced by the stearic radicle ($C_{18}H_{35}O$) and the oleic radicle ($C_{18}H_{33}O$).

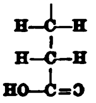
Glycin, sarcosin, lactic acid, leucin, tyrosin, taurin, and hippuric acid are of parallel constitution with members of the fatty acid series already considered, as exhibited in the subjoined table, the amidogen radicle NH_2 taking the place of H in the hydrocarbon radicle or a hydrocarbon radicle replacing H in the amidogen radicle; tyrosin and hippuric acid include a benzoic nucleus, and belong therefore to aromatic bodies; in taurin the sulphur group $SO_2.OH$ replaces the carbon group CO.OH.

Formic acid 			**Taurin or amido-isethionic acid** 
Acetic acid 	**Glycin or amido-acetic acid** 	**Sarcosin or methyl-amido-acetic acid** 	**Hippuric acid or benzyl-amido-acetic acid** 

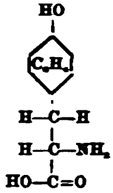
Propionic acid



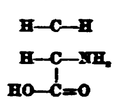
Lactic acid or hydroxy-propionic acid



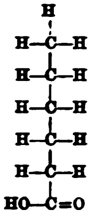
Tyrosin or hydroxy-phenyl-amido-propionic acid



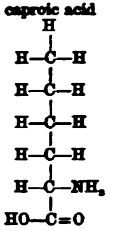
Cystin or sulphamido-propionic acid



Caproic acid



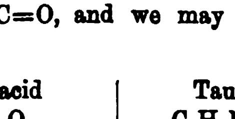
Leucin or amido-caproic acid



Other substances of physiological interest—in particular, uric acid and allied substances—being probably some of the chemical fragments of disintegrated proteid, cannot be arranged in definite series, and are in many cases of unknown or of doubtful structure. We shall, therefore, merely enumerate these bodies, giving their hypothetical constitutional formulæ; and drawing attention to the parallel relations of glycin and of taurin in hippuric and in the biliary acids.

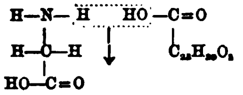
Glycin and benzoic acid form hippuric acid and water.

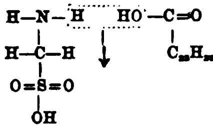
$$C_2H_5NO_2 + \quad C_7H_6O_2 \quad = \quad C_7H_9NO_3 \quad + \quad H_2O$$



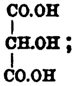
Similar conjugations are effected between glycin and cholic acid, and between taurin and cholic acid; but we have not the data for constructing a graphic formula of cholic acid; it probably contains, however, the group HO—C=O, and we may therefore represent the relations as follows:—

Glycin and cholic acid	Taurin and cholic acid
$C_2H_5NO_2 + C_{24}H_{40}O_5$	$C_2H_7NSO_3 + C_{24}H_{40}O_5$
form	form
Glycocholic acid and water	Taurocholic acid and water
$C_{26}H_{43}NO_6 \quad + \quad H_2O$	$C_{26}H_{45}NSO_7 \quad + \quad H_2O$



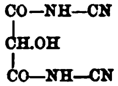


Uric acid, $C_5H_4N_4O_3$.—Of several schemata which have been proposed for uric acid, the simplest is that representing it as a diureide of tartronic acid: *tartronic acid,*



$\begin{array}{l}\text{CO.OH}\\ \vert\\ \text{CH.OH}\\ \vert\\ \text{CO.OH}\end{array}$

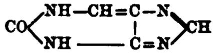
; *uric acid,*



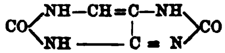
$\begin{array}{l}\text{CO—NH—CN}\\ \vert\\ \text{CH.OH}\\ \vert\\ \text{CO—NH—CN}\end{array}$

Cyanuric acid, $C_3H_3N_3O_3$, or $(CN)_3\,(OH)_3$; oxaluric acid, $C_3H_4N_2O_4$; allantoin, $C_4H_6N_4O_3$; xanthin, $C_5H_4N_4O_2$; hypoxanthin, $C_5H_4N_4O$; guanin, $C_5H_5N_5O$, guanidin, $C_3H_5N_3$, are bodies closely related to uric acid.

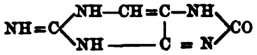
Hypoxanthin or sarcin, $C_5H_4N_4O$ . .



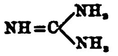
Xanthin, $C_5H_4N_4O_2$ . . . .



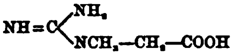
Guanin, $C_5H_5N_5O$ . . . .



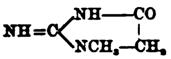
Guanidin, CH_5N_3 . . . .



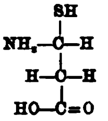
Creatin, methylglycocyamine, or methyl-guanido-acetic acid, $C_4H_9N_3O_2$ . .



Creatinin, or methylglycocyamidine, $C_4H_7N_3O$ . . . .

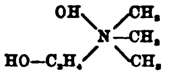


Cystin, $C_3H_7NSO_2$, is constituted on the lactic acid type; it is an amido-lactic acid in which S takes the place of O.



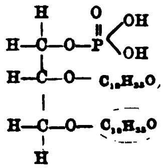
$$\begin{array}{c}\text{SH}\\ \vert\\ \text{NH}_2\text{—C—H}\\ \vert\\ \text{H—C—H}\\ \vert\\ \text{HO—C=O}\end{array}$$

Neurin or cholin . . . .

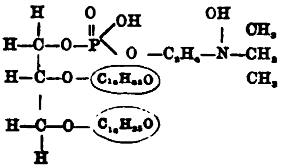


Neurin

Lecithin, $C_{44}H_{90}NPO_9$.—There are several lecithins or phosphorised fats; the most common is the distearyl glycerin phosphate of neurin, which may be represented as under—



Distearyl glycerin phosphate

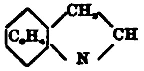


Distearyl glycerin phosphate of neurin

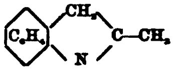
Aromatic compounds

Tyrosin and **hippuric acid** have already been represented (pp. 573, 574).

Indol, C_8H_7N . . . .

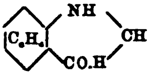


Skatol, C_9H_9N, or methyl indol . . .

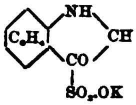


Potassium indoxyl sulphate, $C_8H_6NKSO_4$, so-called '*indican*' of urine, derived from indol.

Indoxyl

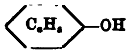


Potassium indoxyl sulphate

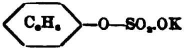


Potassium phenyl sulphate, $C_6H_5KSO_4$, derived from phenol.

Phenol

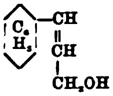


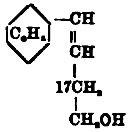
Potassium phenyl sulphate



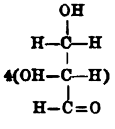
These are the aromatic sulphates alluded to on p. 240.

Cholesterin is a homologue of cinnamyl alcohol, $C_{26}H_{44}O$.



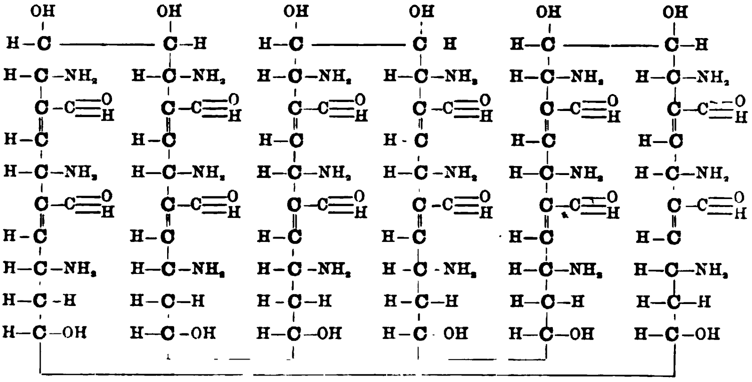


Carbohydrates.—The chemical constitution of the carbohydrates is almost entirely conjectural; we have no right to assign structural formulæ to starch, dextrin or cane-sugar; we may at most *suppose* that dextrose is an aldehyde of the hex-acid alcohol mannite; in which case its structural formula might be represented by



$$\begin{array}{c} OH \\ | \\ H-C-H \\ | \\ 4(OH-C-H) \\ | \\ H-C=O \end{array}$$

Proteids.—The structural formula of proteids is altogether conjectural, and that quoted below is given simply to emphasise the points alluded to in the Introduction, where we learned that proteid is the chemical centre of living matter—a large complex molecule which may take many shapes, and of which the constituent atoms or groups of atoms may 'hold hands' in many different ways, or hold out hands to other molecules with very different effects; a very slight shuffling of the molecule will convert a proteid food into a proteid poison, as we learned in the consideration of albumose (p. 194); attention may be drawn to the conceivable combinations within the chemical range of such a molecule—(1) the amidogen group—NH_2 in relation to urea and other simple nitrogenous bodies; (2) the excess of carbon and of hydrogen in relation to the deposition of carbohydrate or of fat; (3) the *possibility* of a grouping into an aldehyde radicle $H{-}\underset{|}{C}{=}O$ or into a cyanogen radicle —CN, in relation to the possible mode of action of *living* proteid.



A proteid molecule.

III.—UNITS OF MEASUREMENT

French Measures of Length, Weight, and Volume

1 millimètre = $\frac{1}{10}$ centimètre = $\frac{1}{1000}$ mètre.
1 centimètre = $\frac{1}{100}$ mètre.
1 micromillimètre (1 μ) = $\frac{1}{1000}$ millimètre.
1 litre = 1000 centimètres cubes (1000 c.c.)

Relation between volume and weight

1 c.c. = 1 gramme.
1 milligramme = $\frac{1}{1000}$ gramme.
1 kilogramme = 1000 grammes.

Relations between English and French Measures

Length. English to French

1 inch = 2·539954 centimètres.
1 foot = 30·479449 „
1 yard = 91·438347 „
1 mile = 1609·315 mètres.

(*To convert inches into centimètres multiply by* $\frac{33}{13}$.)

Length. French to English

1 centimètre = 0·39371 inch.
1 mètre = 39·37079 inches.
1 micromillimètre = 0·00003937 inch.

(To convert centimètres into inches multiply by $\frac{13}{33}$.)

Weight. English to French

1 grain = 0·0648 gramme.
1 ounce = 28·3495 grammes.
1 pound = 453·592 ,,
1 stone = 6·35 kilogrammes.
1 cwt. = 50·8 ,,
1 ton = 1016 ,,

Weight. French to English

1 gramme = 15·432349 grains.
1 kilogramme = 2·2046213 pounds
or about 35 ounces.
1 milligramme = 0·015432 grain.

Volume. English to French

1 cubic inch = 16·3861759 centimètres cubes.
1 fluid ounce = 28·3495 ,,
1 pint = 567 ,,
1 cubic foot = 28·3153 litres.

Volume. French to English

1 centimètre cube = 0·061027 cubic inch.
1 litre (1000 c.c.) = 61·027 cubic inches
or 35 fluid ounces
or $1\frac{3}{4}$ pints.
1 mètre cube (1000 litres) = 35·3 cubic feet.

Measures of Surface

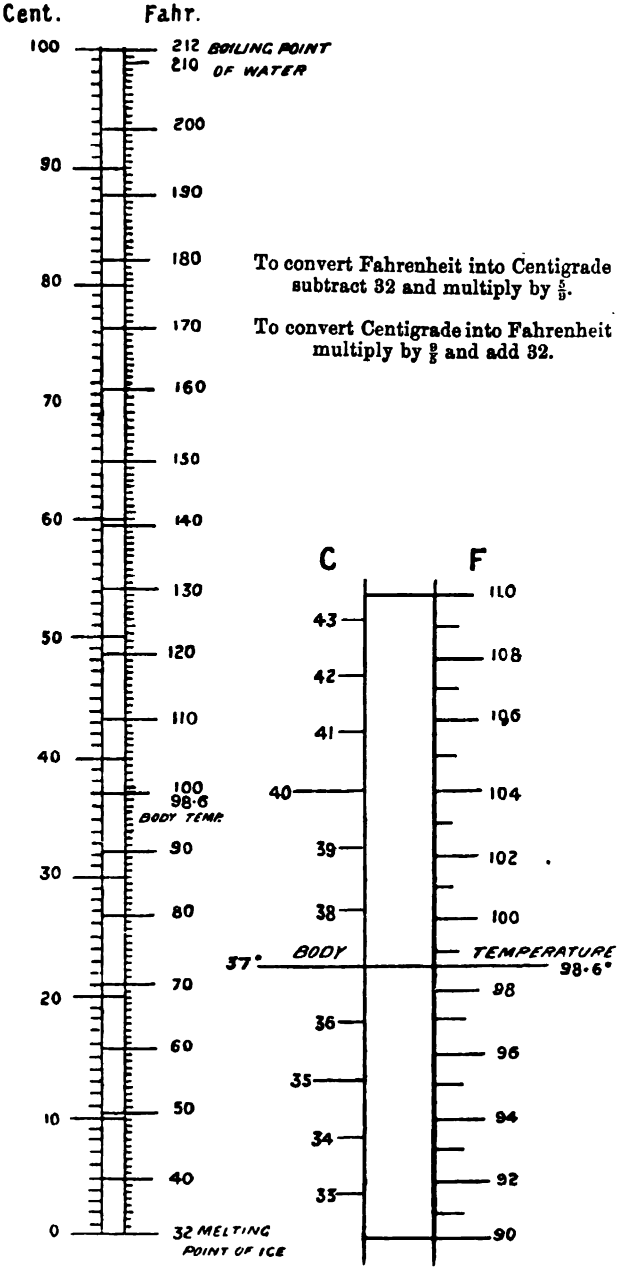
1 square mètre = about 1550 square inches
or 10,000 square centimètres or 10·75 square feet.
1 square inch = about 6·45 square centimètres.
1 square foot = about 930 ,, ,,

Measures of Energy

1 kilogrammètre = about 7·24 foot-pounds.
1 foot-pound = ,, 0·1381 KgM.
1 foot-ton = ,, 310 KgMs.

Mechanical Equivalent of Heat

1 kilocalorie = 424 kilogrammètres.
(or 423·985).



To convert Fahrenheit into Centigrade subtract 32 and multiply by $\frac{5}{9}$.

To convert Centigrade into Fahrenheit multiply by $\frac{9}{5}$ and add 32.

FIG. 293.—CENTIGRADE AND FAHRENHEIT THERMOMETER SCALES.

Approximate solubilities in water at 15° to 18° C. of some salts in frequent use

Sodium chloride	36 per 100
Sodium sulphate	50 „
Ammonium chloride	36 „
Ammonium sulphate	50 „
Magnesium sulphate	125 „
Zinc sulphate	160 „

Volumes of

1 grm. hydrogen = 11160 c.c.
„ oxygen = 697 „
„ nitrogen = 797 „
„ carbon dioxide = 507 „
„ air = 775 „
„ water vapour = 1240 „

Weights of

1000 c.c. hydrogen = 0·0895 grm.
„ oxygen = 1·43 „
„ nitrogen = 1·25 „
„ carbon dioxide = 1·97 „
„ air = 1·29 „
„ water vapour = 0·82 „

Coefficient of expansion of gases

$\frac{1}{273}$ or 0·00366 per 1° C.

ADDENDA

Page 11, *line* 8.—Before 'μ' add '2.'

Page 114.—The view that lymph is a filtrate from the blood, varying in amount with blood-pressure and with movements (Ludwig), is modified by Heidenhain's recent observations, and we must admit that, in addition to *filtration*, a true *secretion* of lymph occurs from the cells of the capillaries and of the tissues. Compare with renal secretion, p. 228.

Page 360.—Many substances excite both muscle and nerve; ammonia and dilute acids act best when directly applied to muscle, while strong glycerine or common salt is more suitable for the excitation of nerve.

BIBLIOGRAPHY

The chief periodical literature of the last half-century is contained in—

The Journal of Physiology (Foster), *from* 1878.
Journal of Anatomy and Physiology (Humphry, Turner, and M'Kendrick), *from* 1868.
Proceedings and Transactions of the Royal Society (Müller), 1834 *to* 1858.
Archiv für Anatomie und Physiologie (Du Bois-Reymond), *from* 1859.
Ludwig's Arbeiten, *Leipsig, from* 1866 *to* 1877 (*continued from* 1877 *in Du Bois-Reymond's Archiv*).
Archiv für die gesammte Physiologie (Pflüger), *from* 1868.
Zeitschrift für Biologie (Kühne u. Voit), *from* 1865.
Physiologisches Centralblatt (Exner u. Gad), *from* 1887.
Archiv für path. Anat. und Physiologie (Virchow), (*Index in* 1885), *from* 1847.
Archiv für exp. Pathol. und Pharmacie (Naunyn u. Schmiedeberg), *from* 1873.
Zeitschrift für physiol. Chemie (Hoppe-Seyler), *from* 1877.
Journal de Physiol. Expérimentale (Magendie), *from* 1821 *to* 1831.
Journal de la Physiologie (Brown-Séquard), *from* 1858 *to* 1863.
Archives de Physiologie (Brown-Séquard), (*Index in* 1883), *from* 1868.
Journal de l'Anat. et de la Physiol. (Robin, Pouchet), *from* 1864.
Comptes Rendus de l'Acad. des Sciences, *from* 1835.
Comptes Rendus de la Société de Biologie, *from* 1850.
Sitzungsberichte d. Acad. d. Wissenschaften, Berlin, *from* 1836; **Wien,** *from* 1848.
Archives Néerlandaises, *from* 1866.
Archives Italiennes, *from* 1882.
Skandinavisches Archiv für Physiologie (Holmgren), *from* 1889.

And for general references or abstracts—

Schmidt's Jahrbücher (*from* 1834); **Canstadt's** Jahresbericht; **Hoffmann und Schwalbe's** Jahresbericht (*from* 1873; *Index in* 1886); **Maly's** Jahresbericht (for physiological chemistry); **Hayem,** Revue des Sciences Médicales.

I. GENERAL PHYSIOLOGY. PROTOPLASM

Lavoisier, Mémoires de l'Académie des Sciences, *Paris,* 1787–89.
Bichat, Recherches sur la Vie et la Mort, 1805.
Schwann, Animal cells, *Microsc. Untersuchungen,* 1839.
Schleiden, Vegetable cells, *Phytogenesis* (*Syd. Soc. Trans.*), 1839.

Virchow, Die Cellularpathologie, 1858.

Liebig, Die organ. Chemie, i. Physiol. u. Pathol., 1842.

Mulder, The Chemistry of Veget. and Animal Physiol. (*Transl.*), 1849.

Mayer, Conservation of energy, *Die organische Bewegung und Stoffwechsel*, Heilbronn, 1845.

Helmholtz, Conservation of energy, *Ueber die Erhaltung der Kraft*, Berlin, 1847; reprint in *Ostwald's Klassiker d. exacten Wissenschaften*, 1889.

Paget, Surgical Pathology, 1st ed. 1853; 3rd edit. 1870.

Darwin, Origin of Species, 1859.

Kühne, Protoplasma u. Contractilität, *Leipsig*, 1864.

Engelmann, Protoplasm and oxygen, *Pflüger's Archiv*, vols. ii. xxv. xxvi., 1869–81.

Pflüger, Physiological combustion, Cyanogen theory, *ibid.*, vol. x., 1875.

Claude Bernard, Physiologie générale, *Paris*, 1872.

—— Phénomènes de la Vie, *Paris*, 1878–9.

Loew u. Bokorny, Die chem. Kraftquelle im lebend. Protoplasma, *Munich*, 1882.

Weissmann, Die Continuität des Keimplasmas, *Jena*, 1885, *Transl. by Poulton, Schönland, and Shipley*, Oxford, 1889.

Hering, Zur Theorie der Vorgänge in der lebendigen Substanz, *Prag*, 1888.

II. BLOOD

Hewson, Corpuscles, Jugular vein coagulation, *Phil. Trans. R. S.*, 1770; *Exper. Inquiries* (reprinted), London, 1877.

Denis, Plasmine, &c., *Rech. Exp. sur le Sang*, Paris, 1830; *Mémoire sur le Sang*, Paris, 1838.

Buchanan, Coagulation, *Lond. Med. Gaz.*, 1831, 1845; *J. of Physiol.* (repr.), 1879.

Gulliver, Size of blood-corpuscles, *Gerber's General Anatomy*, London, 1842.

Wharton Jones, Amœboid movement, *Phil. Trans. R. S.*, 1846.

Waller, Emigration, *Philos. Magazine*, London, 1846.

Cohnheim, Emigration, *Virchow's Archiv*, 1867.

K. Balogh, Emigration, *ibid.*, 1868.

Panum, Serum-casein, *ibid.*, 1851.

Welcker, Amount of blood corpuscles, *Arch. des Vereins zu Göttingen*, 1854; *Zeitschr. f. rat. Med.*, vol. iv., 1858; vol. xx., 1863.

Lister, Jugular vein experiment, *Phil. Trans. R. S.*, 1863.

Brücke, Zooid and œcoid, *Wien. Sitzungsberichte*, 1867.

Binz. Quinine and leucocytes, *Virchow's Archiv*, 1864; *Du Bois-Reymond's Arch.*, 1885; *Das Wesen der Chininwirkung*, Berlin, 1875.

Funke, Hæmoglobin crystals, *Zeitsch. f. rat. Med.*, *Atlas*, 1852.

Teichmann, Hæmatin, *Zeitschr. f. rat. Med.*, 1856.

Hoppe-Seyler, Hb and derivatives, *Centralbl. f. med. Wiss.*, 1864, 1865.

Stokes, Hb reduction, *Phil. Mag.*, 1864.

Preyer, Der Blutcrystalle, *Ann. d. Chemie*, 1866; Jena, 1871.

Hüfner, Spectroscope, *J. f. pract. Chemie*, 1877.

Macmunn, Spectroscope, *Phil. Trans. R. S.*, 1885–86; *J. of Phys.*, vols. vi. viii.

Malassez, Blood-counter, *Arch. de Physiol.*, 1874.

—— Number of corpuscles, *Comptes Rendus de l'Acad. des Sciences*, 1872, 1877.

Gowers, Hæmacytometer, *Lancet*, 1877.

Jones, S.G. of blood, *J. of Phys.*, vol. viii., 1887.

A. Schmidt, Coagulation, *Du Bois-Reymond's Archiv*, 1862.

—— Leucocytes, *Pflüger's Archiv*, vols. v. vi. ix. xi., 1872–5; *Archives de Physiologie*, 1882.

Wooldridge, Coagulation, *Du Bois-Reymond's Arch.*, 1883; *J. of Phys.*, vol. iv., 1883.
—— Injection of thyroid and testis extracts, *Du Bois-Reymond's Arch.*, 1886.
—— The Nature of Coagulation, *London*, 1888.
Hayem, Blood-corpuscles, *Comptes Rendus Ac. d. Sc.*, 1877; *Du Sang*, Paris, 1890.
Bizzozero, *Handb. d. klin. Microscopie*, Erlangen, 1887.
Neumann, Blood and bone marrow, *Med. Centralb.* 1868; *Arch. f. Heilkunde*, 1874.
Metschnikoff, Phagocytes, *Virchow's Archiv*, 1884.
Hammarsten, Serum proteids, *Pflüger's Arch.*, vols. xvii. xix. xxii. xxiv., 1877, 1881.
Halliburton, Serum proteids, *J. of Phys.*, vol. v., 1884.
—— Fibrin ferment, *ibid.*, vol. ix., 1888.
Schmidt-Mülheim, Peptones and coagulation, *Du Bois-Reymond's Archiv*, 1879.
Fano, Peptones, *ibid.*, 1881.
Pollitzer, Peptones and albumoses, *J. of Phys.*, vol. vii., 1886.
Haycraft, Leech extract, *ibid.*, vol. v., 1884.
Dickinson, Leech albumose, *ibid.*, vol. xi., 1890.
Heidenhain, Lymph secretion, *Pflüger's Archiv*, vol. xlix., 1891.

III. CIRCULATION

Servetus, Pulmonary circulation, *Restitutio Christianismi*, 1553.
Harvey, Systemic circulation, *De Motu Cordis et Sanguinis*, Frankfort, 1628.
Malpighi, Capillaries, *De Pulmonibus*, Bonon., 1661.
Hales, Blood-pressure, *Statical Essays*, 1732.
Hering, Speed of circulation, *Tiedemann's Zeitschr. f. Physiol.*, vol. iii., 1829, 1832.
Hermann, Rapidity of circulation, *Pflüger's Archiv*, vol. xxxiii. p. 169, 1884.
Weber, Wellenlehre (1850), *Ostwald's Class. d. exakten Wissensch.* (rep.), 1889.
Donders, Pressure and capacity, *Physiologie des Menschen*, Leipsig, 1856.
Erichsen, Ligature of coronaries, *Edin. Med. and Surg. Journ.*, 1845.
Stannius, Frog heart, *Arch. f. Anat. u. Phys.*, 1852.
Bowditch (Leipsig), 'Staircase' beats, *Ludwig's Arbeiten*, 1871.
Foster, Heart of snails, *Pflüger's Archiv*, vol. v. p. 191, 1872; *Proc. R. S.*, 1875.
Waller and Reid, Excised mammalian heart, *Phil. Trans. R. S.*, 1887.
McWilliam, Mammalian heart, *J. of Phys.*, vol. ix., 1888.
Schmiedeberg, Muscarin, *Ludwig's Arbeiten*, 1870.
Langley and Dickinson, Nicotin, *Proc. R. S.*, 1889; *J. of Physiol.*, 1890.
Poiseuille, Velocity in capillaries, *Mém. de l'Académie des Sciences*, 1835.
Chauveau, Bertolus et Laroyenne, Hæmodromometer, *J. de la Phys.*, 1860.
Chauveau et Marey, Appareils et Expériences Cardiographiques, *Paris*, 1863.
Dogiel (Leipsig), Stromuhr, *Ludwig's Arbeiten*; *Pflüger's Archiv*, vol. iv., 1867.
Mosso (Leipsig), Plethysmograph, *Ludwig's Arbeiten*, 1875.
—— Cerebral effects, *Diagnostik des Pulses*, *Leipsig*, 1879.
Roy, Spleen contractions. Arterial elasticity, Oncograph, *J. of Phys.*, vol. iii., 1880.
Heidenhain, Pressure and flow, Int. and ext. temp., *Pflüger's Arch.*, vol. iii., 1870.
Dogiel and Kowalewsky, Blood-flow in asphyxia, *ibid.*, vol. iii., 1870.
Slaviansky (Leipsig), Pressure and flow, *Ludwig's Arbeiten*, 1873.
Nasse, Outflow of blood, *Pflüger's Archiv*, vol. xxii., 1880.
Howell and Donaldson, Systolic quantity, *Proc. R. S.*, vol. xxxv. p. 271, 1883.
Cybulski, Blood-stream, Photohæmotachometer, *Pflüger's Arch.*, vol. xxxvii., 1885.
Stolnikow (Leipsig), Aortic current, *Du Bois-Reymond's Arch.*, 1886.
de Jäger, Blood-flow, *Pflüger's Arch.*, vols. xx.-xxxvi., 1879-85; *J. of Phys.*, vol. vii., 1886.

Pawlow (Leipsig), Aortic stromuhr, Non-coag. of blood, *Du Bois-Reymond's Arch.*, 1887.

Goltz and Gaule, Cardiac suction, *Pflüger's Archiv*, vol. xvii. p. 100, 1878.

Keyt, Pulse-wave, *Journ. of the American Medical Association*, 1883.

Landois, Hæmautogram, *Pflüger's Arch.*, vol. ix., 1874.

Marey, Méthode graphique de la Circulation du Sang, *Paris*, 1878.

Martin and Sedgwick, Coronary pulse, *J. of Physiol.*, vol. iii., 1880–2.

Waller, Pulse-wave, *ibid.*, 1880–2.

v. Frey, Reflected pulse-waves, *Du Bois-Reymond's Archiv*, 1890.

Hürthle, Reflected pulse-waves, *Pflüger's Archiv*, vol. xliv., 1889, 1891.

A. Fick, Reflected pulse-waves, *ibid.*, 1891.

v. Kries, Capillary pressure, *Ludwig's Arbeiten*, 1875.

Roy and Brown, Capillary pressure, *J. of Phys.*, vol. ii., 1879.

Merunowicz (Leipsig), Serum ash and frog heart, *Ludwig's Arbeiten*, 1875.

Gaule (Leipsig), Peptones and frog heart, *Du Bois-Reymond's Archiv*, 1878.

Ringer, Frog heart and salts, Muscarin and pilocarpin, *J. of Phys.*, vols. i.–vi., 1878–85.

Popoff (**Kronecker**), Serum-albumin perfusion, *Zeitsch. f. Biol.*, 1889.

Brinck (**Kronecker**), Serum-albumin perfusion, *ibid.*, 1889.

Gaskell, Acids and alkalies and heart tone, *J. of Phys.*, vol. iii., 1880–2.

Panizza, Sopra il systema linfatico de' retilli, *Pavia*, 1833.

J. Müller, Lymph hearts, *Phil. Trans.*, 1833; *Müller's Archiv*, 1834.

Priestley, Lymph hearts (bibliog.), *J. of Phys.*, vol. i., 1878.

Weber, Vagus inhibition, *Wagner's Handwörterbuch*, 1846.

Budge, Vagus inhibition, *Müller's Archiv*, 1846.

Henle, Criminal's vagus, 1852.

Waller, Vagus excitation on man, Spinal accessory, *Proc. R. S.*, 1861.

Goltz, Reflex vagus inhibition, *Virchow's Arch.*, 1863.

Czermak, Vagus excitation on man, *Schmidt's Jahrberichte*, vol. cxliii. p. 273, 1868.

Donders, Vagus latency, *Pflüger's Archiv*, vol. i., 1868.

Baxt (Leipsig), Accelerators, *Ludwig's Arbeiten*, 1875–6; *Du Bois-Reymond's Arch.*, 1878.

F. Franc, Accelerator nerves, *Trav. de Marey*, 1878, 1879.

Schiff, Accelerators in vagus, *Pflüger's Arch.*, vol. xviii., 1878.

Gamgee and Priestley, Excitation of both vagi, *J. of Phys.*, vol. i., 1878.

Heidenhain, Two kinds of vagus fibre, *Pflüger's Archiv*, vol. xxvii., 1882.

Wooldridge (Leipsig), Nerves in ventricles, *Du Bois-Reymond's Arch.*, 1883.

Meltzer, Irradiation and swallowing inhibition, *ibid.*, 1883.

Kronecker and Schmey, Inhibitory spot, *Deut. med. Wochensch.*, 1884.

Gaskell, Trophic action of vagus, *Phil. Trans. R. S.*, 1882.

—— Accelerators in frog's vagus, *J. of Phys.*, vol. v., 1884.

—— Visceral nerves, *ibid.*, vol. vii., 1886.

—— Electrical changes, Muscarin, *ibid.*, vol. viii., 1887.

Brown-Séquard, Cervical sympathetic, *Philadelphia Medical Examiner*, 1852.

Claude Bernard, Cervical sympathetic, *Comptes Rendus Acad. Sc.*, p. 472, 1852.

—— Chorda tympani, *Comptes Rendus*, p. 159, 1858; *Liquides de l'Organisme*, 1859.

Waller, Cervical sympathetic, *Comptes Rendus de l'Acad. des Sciences*, 1853.

—— Nerves of extremities, *Proc. R. S.*, 1861.

Wharton Jones, Venous rhythm of bat's wing, *Phil. Trans. R. S.*, 1852; *Med.-Chir. Trans.*, 1853.

Lister, Vasomotor action, *ibid.*, 1858.

Eckhardt, Nervi erigentes, *Beiträge*, vol. iii., 1863.

Echhardt, Trigeminal, *Beiträge*, vol. iv., 1867.
Cyon and Ludwig, The depressor, *Ber. d. Sächs. Ges. d. Wiss.*, 1866.
Owsjannikow (Leipsig), Vasomotor centre, *Ludwig's Arbeiten*, 1871.
Dittmar (Leipsig), Vasomotor centre, *ibid.*, 1873.
Sadler (Leipsig), Vaso-dilatators of muscle, *ibid.*, 1869.
Hafiz (Leipsig), Vaso-dilatators of muscle, *ibid.*, 1870.
Gaskell (Leipsig), Vaso-dilatators of muscle, *ibid.*, 1876.
—— Vaso-dilatators of muscle, *J. of Phys.*, vol. i., 1878.
Goltz, Vaso-dilatation, *Pflüger's Arch.*, vols. ix. xi., 1874–5.
Huizinga, Vasomotor action, *ibid.*, vol. xi. 1875.
Ostroumoff. Vasomotor nerves, *ibid.*, vol. xii., 1876.
Latschenberger and Deahna, Repeated stim. of vasomotors, *ibid.*, vol. xii., 1876.
Dastre and Morat, Cervical sympathetic, *Comptes Rendus*, *J. de Physiol.*, 1880.
Lewaschew, Cutaneous vasomotors, *ibid.*, vol. xxviii., 1882.
Luchsinger, Sudomotor nerves, Cat. pilocarpin and atropin, *ibid.*, vols. xiv.–xviii., 1877–8.
Lichtheim, Die Störungen des Lungenkreislaufs, *Breslau*, 1876.
Waller (Leipsig), Pulmonary vasomotors, *Du Bois-Reymond's Arch.*, 1878.
F. Franc, Pulmonary vasomotors, *C. Rend. Soc. Biol.*, 1880.
Openchowski (Vienna), Pulmonary vasomotors, *Pflüger's Arch.*, vol. xxvii., 1882.
Bradford, Pulmonary vasomotors, *Proc. R. S.*, *J. of Phys.*, vol. x., 1889.
—— Renal vasomotors, *J. of Phys.*, 1889.
Mall (Leipsig), Portal vasomotors, *Du Bois-Reymond's Arch.*, 1890.

IV. RESPIRATION

Priestley, *Phil. Trans. R. S.*, 1776.
Spallanzani, Mémoire sur la Respiration, *Genève*, 1803.
Bunsen, *Ann. d. Chimie*, 1835.
Scharling, *Ann. der Chem. und Pharm.*, 1843.
Sibson, Mechanism of Respiration, *Phil. Trans. R.S.*, 1847.
Hutchinson, Spirometry, *Trans. Med.-Chir. Soc.*, 1848.
Regnault and Reiset, Respiration apparatus, *Ann. de Chim. et de Phys.*, 1849.
E. Smith, Respiration, *Pr. R. S.*, *Trans. R. S.*, 1859.
Pettenkofer and Voit, Respiration apparatus, *Liebig's Annalen*, 1862.
Donders, Dissociation, *Arch. Néerland.*, 1873.
Zuntz, Respiration apparatus, *Du Bois-Reymond's Arch.*, 1889.
Paul Bert, La Pression Barométrique, *Paris*, 1878.
Cyon, Criticism of Paul Bert, *Du Bois-Reymond's Arch.* (*Festschrift*), 1883.
Aubert, CO_2 through skin, *Pflüger's Archiv*, vol. vi., 1872.
Fraenkel, Respiration in fever, *Du Bois-Reymond's Archiv*, 1879.
Magnus, Analysis of blood-gases, *Ann. d. Physik*, 1837 and 1845.
Sczelkow (Ludwig), Blood-gases, *Sitzungsberichte Wien*, 1862.
Schmidt (Ludwig), Blood-gases, *Verh. d. Sächs. Ges. der Wiss.*, Leipsig, 1867.
Ludwig, Blood-gases, *Wien. med. Jahrbücher*, 1865.
Hermann, Unters. ü. d. Stoffwechsel der Muskeln (Gaswechsel), *Berlin*, 1867.
Pflüger (with Finkler, Oertmann, Zuntz, Colosanti), Internal respiration, *Pflüger's Arch.*, vols. xii.–xviii., 1876–8.
Wolffberg (Bonn), Aerotonometer, Pulmonary catheter, *ibid.*, vols. iv. v., 1871, vol. vi., 1872.
Strassburg (Bonn), Aerotonometer, *ibid.*, vol. vi., 1872.
Pflüger, Oxidation, *ibid.*, vol. vi., 1872, vol. x., 1875, vol. xiv., 1877.

Pflüger and Oertmann, Gaseous exchanges of 'salt' frogs, *ibid.*, vol. xv., 1877.
Gaule (Leipsig), CO_2 tension, *Du Bois-Reymond's Archiv*, 1878.
Seegen and Nowak, Exhaled N (?), *Pflüger's Archiv*, vol. xix., 1879.
Ch. Bohr, Blood-gases, *Centralbl. f. Physiol.*, 1887–8; CO_2 and Hb, *Ludwig's Festschrift*, 1887.
—— CO_2 and Hb, *Bull. de l'Acad. Royale Danoise*, 1890.
Ludwig, Effect of respiration on circulation, *Müller's Archiv*, 1847.
Einbrodt, Effect of respiration on circulation, *Moleschott's Unters.*, 1860.
B. Sanderson, Effect of respiration on circulation, *Phil. Trans. R.S.*, 1867.
Fleischl v. Marxow, *Bedeut. d. Herzschl. f. d. Athmung*, Stuttgart, 1887.
Hering and Breuer, Vagus and respiration, *Wiener Sitzungsb.*, 1868.
Guttmann, Vagus and respiration, *Du Bois-Reymond's Arch.*, 1875.
Head (Prag), Nervous regulation of respiration, *J. of Phys.*, vol. x., 1889.
Garcia, The laryngoscope, *Lond., Edinb., and Dubl. Phil. Mag.*, 1855.
Czermak, *Der Kehlkopfspiegel, &c.*, Leipsig, 1860.
Galen (second century), Laryngeal nerves, *Œuvres* (*Daremberg's translation*), Paris, 1854–6.
Krause, Innervation of larynx, *Du Bois-Reymond's Arch.*, 1884.
Semon and Horsley, Innervation of larynx, *British Medical Journal*, 1889.

V. DIGESTION

Engelmann, Contraction of ureter, *Pflüger's Archiv*, vols. ii. and iii. 1869–70.
—— Contraction of intestine, *ibid.*, vol. iv., 1871.
Mosso, Œsophagus, *Moleschott's Untersuchungen*, 1874.
Kronecker and Meltzer, Deglutition, *Du Bois-Reymond's Archiv* (suppl.), 1883.
Ludwig and Spiess, Temp. of saliva, *Wiener Sitzungsberichte*, p. 548, 1857; *Zeitsch. f. rat. Med.*, p. 361, 1858.
Ludwig (Becker and Rahn), Ueber dem Speichel (1851), *Ostwald's Classiker d. exacten Wissensch.* (reprint), 1890.
Pflüger, Salivary nerve-ends (?), *Centralbl. med. Wiss.*, 1865.
Kupffer, Salivary nerve-ends, *Ludwig's Festgabe*, 1874.
Heidenhain, Salivary glands, Trophic nerves, *Pflüger's Archiv*, vol. xvii., 1878.
—— Secretion, *Hermann's Handbuch der Physiologie*, vol. v., 1883.
—— Pilocarpin, atropin, &c., *Pflüger's Archiv*, vol. v., 1872.
Langley (Heidelberg), Pilocarpin and atropin, *J. of Physiol.* vol. i., 1878–82.
Langley, Salivary glands, *ibid.*, vols. i. and ii., 1878–9; vols. ix. and x., 1888–9.
—— Paralytic secretion, *ibid.*, vol. vi., 1885.
—— Mucous granules, *ibid.*, vol. x., 1889.
Spallanzani, Expériences sur la Digestion, *Genève*, 1783.
Schwann, Pepsin, *Müller's Archiv*, p. 90, 1836.
Bidder and Schmidt, Die Verdauungssäfte und der Stoffwechsel, *Leipsig*, 1852.
Brücke, Proteolysis, *Wiener Sitzungsber.*, vols. xxxvii. and xliii., 1859–62.
—— Preparation of pepsin, &c., *Vorlesungen über Physiologie*, 3rd edit., Wein, 1881.
Meissner, Proteolysis, Preparation of pepsin, *Zeitsch. f. rat. Med.*, vols. vii.–xiv., 1859–62.
Pavy, Stomach self-digestion, *Phil. Trans. R. S.*, 1863.
v. Wittich, Peptic glycerine, *Pflüger's Arch.*, vols. ii. iii., 1869–70.
Grützner, Estimation of pepsin, *ibid.*, vol. viii., 1874.
—— Ferments, *ibid.*, vol. xvii., 1878; vol. xx., 1879.
Kühne, Proteolysis, Preparation of pepsin, *Verh. nat. med. Ver. Heidelberg*, 1876.
Maly, Digestive juices, *Hermann's Handbuch*, vol. v., 1883.

Uffelmann, Tests for gastric acids, *Deut. Arch. f. klin. Med.*, 1880; *Zeitsch. f. klin. Med.*, 1884.

Langley and Sewall, Pepsin glands, *J. of Physiology*, vol. ii., 1879.

Langley, Pepsin glands, *ibid.*, vol. iii. 1880; *Phil. Trans. R. S.*, 1881.

Langley and Edkins, Pepsinogen and pepsin, *J. of Physiology*, vol. vii., 1886.

Heidenhain, Gastric cæca, *Pflüger's Archiv*, vols. xviii. and xix., 1878.

Schiff, Load theory, *ibid.*, vol. xxviii., 1882.

Ogata, Gastric digestion, *Du Bois-Reymond's Archiv*, 1883.

Kühne (with Chittenden and Neumeister), Proteid digestion, *Zeitsch. f. Biol.*, vols. xix.–xxiv., 1883–86.

Wooldridge, Anthrax albumose, *Du Bois-Reymond's Arch.*, 1888.

Wolfenden, Proteids of cobra venom, *J. of Physiol.*, vol. vii., 1886.

Martin, Anthrax albumose, *Proc. R. S.*, 1890.

—— Proteids of papaïn, *ibid.*, vol. xliii. p. 331.

Hankin, Protective albumose, *British Medical Journal*, 1890.

Brieger, Unters. über Ptomaine, *Berlin*, 1886.

Blondlot, Essai sur les fonctions du foie, *Paris*, 1846.

Chrzonszczewsky, Bile ducts, *Virchow's Archiv*, 1866.

Hammarsten, Influence of bile on gastric digestion, *Pflüger's Arch.*, vol. iii., 1870.

Rutherford and Vignal, Bile, Cholagogues, *Phil. Trans. R. S. Edinb.*, 1870.

v. Basch, Biliary pressure, *Ludwig's Arbeiten*, 1875.

Copeman and Winston, Biliary fistula, *J. of Physiology*, 1889.

Martin and Williams, Influence of bile on pancreatic digests, *Proc. R. S.*, vol. xlv. p. 358, 1889; vol. xlviii. p. 160, 1890.

Shore and Jones, Tubular structure of liver, *J. of Physiol.*, vol. x., 1889.

Corvisart, Sur une fonction peu connue du pancréas, *Gaz. Hebdom.*, 1857, 1860; *Union Médicale*, 1861.

—— Sur une fonction puissante et méconnue du pancréas, *Gas. Médicale*, 1864.

Bernard, Mémoire sur le pancréas, *Paris*, 1856.

Kühne, Pancreas, *Virchow's Archiv*, 1867.

—— *Lehrb. d. physiol. Chemie*, Leipsig, 1868.

Bernstein, Pancreatic secretion, *Ludwig's Arbeiten*, 1869.

Heidenhain, Pancreas, *ibid.*, vol. x., 1875.

Kühne, Trypsin, *Verh. d. Heidelberg. nat. med. Vereins*, 1876.

Kühne and Lea, Pancreas granules, *Untersuchungen Heidelberg*, vol. i., 1877.

Minkowski and v. Mering, Pancreas and diabetes, *Arch. f. exp. Path. und Pharm.*, 1890.

Herzen, Spleen and digestion, *Centralbl. f. med. Wiss.*, 1877; *Pflüger's Archiv*, vol. xxx., 1883.

Graham, Osmose, *Phil. Trans. R. S.*, 1854-61.

Bernard, Absorption, *Substances Toxiques*, Paris, 1857.

E. W. Reid, Absorption, Frog's skin, *J. of Physiology*, 1890.

Cazeneuve and Livon, Bladder absorption, *Comptes Rendus*, 1878.

Brücke, Pump action of villi, *Wiener Sitzungsberichte*, 1851.

Thiry, Intestinal fistula, *ibid.*, 1864.

Moreau, Paralytic secretion of intestine, *Centralbl. med. Wiss.*, 1868.

T. Munk, Fat absorption, *Virchow's Arch.*, 1884–5.

Röhmann, Intestinal absorption, *Pflüger's Archiv*, vol. xli., 1887.

Heidenhain, Intestinal structure and function (Bibl.), *ibid.*, vol. xliii., 1888.

Bernard, Glycogenesis, *Nouvelle Fonction du Foie*, Paris, 1853; *Leçons de Physiologie*, 1855; *Leçons sur le Diabète*, 1877.

v. Hensen, Liver and sugar, *Verh. Würzb.*, 1856; *Virchow's Arch.*, vol. xi., 1857.

MacDonnell, Diabetic sugar, Liver, *Dublin Quart. J.*, 1859; *Observation on the Functions of the Liver*, 1865.
Pavy, Glycogen, *Phil. Trans. R. S.*, 1860; *On Diabetes*, London, 1862.
Seegen, Sugar, &c., *Pflüger's Arch.*, 1879–85; *Studien ü. Stoffwechsel*, Berlin, 1887.

VI. AND VII. KIDNEY, NUTRITION, ANIMAL HEAT

Bowman, Structure and function of kidney, *Phil. Trans. R. S.*, 1842.
Ludwig, Filtration theory, *Lehrbuch der Physiologie*, 1856.
Heidenhain, Kidney, *Pflüger's Arch.*, vol. ix., 1874.
Nussbaum, Amphibian kidney, *ibid.*, vols. xvi. and xvii., 1878.
Adami, Amphibian kidney, *J. of Physiol.*, vol. vi., 1885.
Roy and Cohnheim, Kidney volume experiments, *Virch. Arch.*, vol. xcii., 1883.
Mosso and Pellacani, Bladder contraction, *Arch. Ital. de Biol.*, 1882.
Heidenhain and Colberg, Sphincter vesicæ, *Du Bois-Reymond's Arch.*, 1858.
Kjeldahl, Estimation of N, *Zeitsch. f. Anal. Chemie*, 1883.
Bunge and Schmiedeberg, Hippuric acid, *Arch. f. exp. Path. u. Pharm.*, vol. vi., 1876.
v. Schröder, Urea, *ibid.*, 1885.
Chossat, Recherches exp. sur l'Inanition, *Paris*, 1843.
Parkes, Food tables, *Manual of Hygiene* (7th ed.), 1887.
Ashdown, Glycuronic acid, *Laboratory Reports R. C. P. Edinb.*, vol. ii., 1890.
König, Chemie der menschl. Nahrungs- und Genussmittel, *Berlin* (3rd ed.), 1889.
Bunge, Physiological Chemistry (transl. by Wooldridge), *London*, 1890.
Lawes and Gilbert, Fat storage, *Phil. Trans. R. S.*, 1859.
Fick and Wislicenus, Ascent of Faulhorn, *Phil. Mag.*, vol. xxxi., 1866.
Pavy, Nitrogen excretion of pedestrians, *Lancet*, pp. 319, 353, 1876.
North, Nitrogen excretion of pedestrians, *J. of Physiol.*, vol. i., 1878.
Page, Nitrogen excretion, *ibid.*, vol. ii., 1879–80.
Pettenkofer and Voit, Balance of nutrition, *Hermann's Handb.*, vol. vi., 1881.
Zuntz and von Mering, Food and oxidation, *Pflüger's Arch.*, vol. xxxii., 1883.
Paton and Stockman, Starvation metabolism, *Proc. R. S. Edinb.*, 1889.
Argutinsky, Work and nitrogen, *Pflüger's Archiv*, vol. xlix., 1890.
Pflüger, Proteid and work, *ibid.*, vol. l., 1891.
Paton, Musc. work and proteid metabolism, *Laborat. Reports R. C. P. Edinb.*, 1891,
Paton and Balfour, Bile, *ibid.*, 1891.
Béclard, Work and heat, *Comptes Rendus d. l'Ac. des Sc.*, 1860.
Liebermeister, Ext. and int. tempi., *Du Bois-Reymond's Arch.*, 1860.
Naunyn and Quinke, Temp. after cord section, *ibid.*, 1869.
Heidenhain, Post-mortem heat, &c., *Pflüger's Arch.*, vol. iii., 1870.
Bruck and Gunther (Heidenhain), Post-mortem heat, &c., *ibid.*, vol. iii., 1870.
Röhrig and Zuntz, Heat regulation, *ibid.*, vol. iv., 1871.
Senator, Calorimetry, *Du Bois-Reymond's Arch.*, 1872.
Rosenthal, Der Wärmeregulirung b. d. warmblütigen Thieren, *Erlangen*, 1872.
Eulenburg and Landois, Thermic and vasc. nerves, *Virch.Arch.*, vol. lxviii., 1876.
Rosenthal, Calorimeter, *Du Bois-Reymond's Arch.*, p. 349, 1878.
Kronecker and Meyer, Local temperature, *ibid.*, p. 569, 1879.
Wood, Fever, &c., *Washington*, 1880.
Richet, Heat puncture, *Comptes Rendus*, 1884.
Ott, Heat puncture, *J. of Neur. and Ment. Dis.*, 1884.
Aronsohn and Sachs, Heat centre, Brain, *Pflüger's Arch.*, vol. xxxvii., p. 232, 1885.

Heidenhain, Mech. Leist., Wärmeentwickelung u. Stoffumsatz bei Muskelthätigkeit, *Leipsig*, 1864.

Fick, Muscle heat, *Pflüger's Arch.*, vol. xvi., 1878.

—— Muskelthätigkeit, *Leipsig*, 1882.

Danilewski, Muscle heat, *Pflüger's Arch.*, vols. xxiv. xxx., 1881-2.

Meade Smith, Muscle heat, *Du Bois-Reymond's Arch.*, 1881.

Chauveau, Travail musculaire, *Paris*, 1891.

IX. AND X. MUSCLE AND NERVE

Bowman, Sarcous elements, *Phil. Trans. R. S.*, 1840.

Brown-Séquard, Contractility and circulation, *Compt. Rend. de l'Ac. des Sc.*, 1851.

Stannius, Contractility and circulation, *Arch. f. phys. Heilk.*, vol. xi., 1851.

Bernard, Curare, *Leçons sur les Substances Toxiques*, Paris, 1857.

Guareschi and Mosso, Curare, *Arch. Ital. de Biologie*, vols. ii. and iii., 1882-3.

Ranvier, Red and pale muscle, *Leçons sur le Système Musculaire*, Paris, 1880.

Grützner, Red and pale muscle, *Breslauer ärztliche Zeitschrift*, 1883.

Helmholtz, Latent period of muscle, Rapidity of nerve impulse, *Müller's Archiv*, 1850.

Helmholtz and Baxt, Rapidity of nerve impulse on man, *Ber. d. Berlin. Acad.*, 1867.

Weber, Muscle elasticity, *Wagner's Handwörterbuch*, 1846.

Wertheim, Muscle elasticity, *Ann. d. Chimie et de Phys.*, 1847.

Volckmann, Muscle elasticity, *Müller's Archiv*, 1859.

v. Anrep, Muscle elasticity, *Pflüger's Archiv*, vol. xxi., 1880.

Aeby, Wave of contraction, *Du Bois-Reymond's Arch.*, 1860.

Cash, Length of contraction, *J. of Anat. and Phys.*, 1881.

Mendelssohn, Latent period, *Marey's 'Travaux,'* vol. iv., 1878-9.

Yeo and Cash, Latency of muscle, *J. of Phys.*, vol. iv., 1883.

Tigerstedt, Latency of muscle, *Du Bois-Reymond's Arch.* (suppl.), 1885.

Yeo, Latency of muscle, *J. of Physiol.*, vol. ix., 1888.

B. Sanderson, Latency, *Proc. R. S.*, 1890.

Helmholtz, Muscle tone, *Verh. d. naturh. Vereins z. Heidelberg*, 1868.

Bernstein, Muscle sound by chem. excit., *Pflüger's Archiv*, vol. xi., 1869.

Lovèn, Strychnia tetanus, *Med. Centralbl.*, 1881.

—— Muscle sound; unipolar fallacy, *Du Bois-Reymond's Arch.*, 1881.

Kronecker and Hall, Voluntary contraction, *ibid.*, 1879.

v. Kries, Voluntary contraction, *ibid.*, 1886.

Schäfer, Voluntary tremor, *J. of Phys.*, vol. vii., 1886.

Duchenne, Co-operative antagonism, *Electrisation localisée*, Paris, 1855.

Beaunis, Contraction of antagonists, *Arch. de Physiol.*, 1889.

Demeny, Contraction of antagonists, *ibid.*, 1890.

Kronecker and Stirling, High tetanising frequency, *Du Bois-Reymond's Arch.*, (transl.) *J. of Phys.*, vol. i., 1878.

Gad and Heymans, Isotonic and isometric contractions, *Du Bois-Reymond's Arch.* (suppl.), 1890.

Kronecker, Fatigue curve, *Berichte d. Sächs. Ges. d. Wiss.*, 1870.

Kronecker and Gotch, Tetanus curve, *Du Bois-Reymond's Archiv*, 1880.

Bohr, Tetanus curve, *ibid.*, 1882.

Wedenskii, Telephone and muscle, *ibid.*, 1883; *Arch. de Physiol.*, 1890.

—— Fatigue of nerve, *Centralbl. f. med. Wiss.*, 1884; *Du Bois-Reymond's Archiv*, 1891; *J. of Physiol.*, 1885.

Bowditch, Fatigue of nerve, *Du Bois-Reymond's Archiv*, 1890.
Waller, Fatigue of nerve, Motor end-plate, *Brit. Med. Journal*, 1885–6.
Fick, Human muscle, *Pflüger's Archiv*, vol. xli. xlv., 1887–9.
Mosso, Fatigue of human muscle, *Du Bois-Reymond's Archiv*, 1890.
Helmholtz, Muscle-extractives, *Müller's Arch.*, 1845.
Du Bois-Reymond, Muscle acid, *Gesammelte Abhandlungen*, 1859.
Ranke, Tetanus, *Du Bois-Reymond's Arch.*, 1863; Leipsig, 1865.
Grützner, Pyrogallic acid, *Pflüger's Arch.*, vol. vii., 1873.
Nasse, Glycogen and lactic acid, *ibid.*, vol. ii., 1868.
Boehm, Glycogen and lactic acid, *ibid.*, vol. xxiii., 1880.
Marcuse, Glycogen and lactic acid, *ibid.*, vol. xxxix., 1886.
v. Frey, Muscle respiration, *Du Bois-Reymond's Arch.*, 1885.
Halliburton, Muscle-proteids, *J. of Physiol.*, 1887.
Bierfreund, Rigor mortis, *Pflüger's Arch.*, vol. xliii., 1888.
Rollett, Flexors and extensors, *Wiener Sitzungsber.*, 1874–6.
Du Bois-Reymond, Electrotonic currents, *Untersuchungen ü. thier. Elektr.*, 1848–9.
Pflüger, Electrotonic excitability, Law of contraction, *Unters. ü. d. Physiol. d. Electrotonus*, Berlin, 1859.
Chauveau, Unipolar excitation, *Comptes Rendus d. l'Acad. des Sciences*, 1875.
Tigerstedt, Mechanische Nervenreizung, *Helsingfors*, 1880.
Waller and de Watteville, Electrotonic excitability on man, Motor nerves, *Phil. Trans. R. S.*, 1882.
—— Sensory nerves, *Proc. R. S.*, 1882.
de Watteville, Medical electricity, London, 1884.
Biedermann, Anodic inhibition, *Wiener Sitzungsber.*, 1885.
Hering, Positive after-effect of neg. var., *ibid.*, 1884.
Head, Positive after-effect of neg. var., *Pflüger's Archiv*, vol. xl. 1887.
Nasse, Nerve degeneration, *Müller's Arch.*, p. 405, 1839.
Waller, De- and re-generation of nerve, *ibid.*, 1852.
Engelmann, Nerve degeneration, *Pflüger's Archiv*, vol. xiii., 1876.
—— Discontinuity of axis-cylinder, *ibid.*, vol. xxii., 1880.
Ranvier, De- and re-generation of nerve, *Histol. du Syst. Nerveux*, Paris, 1878.
Vanlair, Dérivation des nerfs, *Arch. de Physiologie*, 1885–6.
S. Mayer, Regeneration of nerve, *Arch. f. Psych.*, 1876; *Prager Zeitsch.*, 1881.
Joseph, Spinal ganglia, *Du Bois-Reymond's Arch.*, 1887.
Exner, Degen. of larynx muscle, *Centralbl. f. Physiol.*, 1889.
Pineles, Trophic action of sup. laryngeal nerve, *Pflüger's Arch.*, vol. xlviii., 1890.
Bert, La greffe animale, *Paris*, 1863.
Kühne, Double conduction, *Zeitsch. f. Biol.*, 1885.

XI. ANIMAL ELECTRICITY

Galvani, De Viribus Electricitatis in motu Musculari, *Bologna*, 1791.
—— Opere del Prof. Luigi Galvani, *Bologna*, 1841.
Aldini, Essai théorique et expérimental sur le Galvanisme, *Paris*, 1804.
Volta, Memoria sull' elletricità animale, 1792.
Matteucci, Essai sur les Phénomènes Electriques des Animaux, *Paris*, 1840.
Du Bois-Reymond, Untersuchungen ü. thier. Elektricität, 1848-4.
Hermann, Hermann's Handbuch, vol. i., 1879.
Bernstein, Neg. var. of electrotonus, *Du Bois-Reymond's Archiv*, p. 596, 1866.
—— Untersuchungen ü. d. Erregungsvorgang, *Heidelberg*, 1871.
Sanderson and Page, Electrical phenomena of frog's heart, *Proc. R. S.*, 1878.
Gotch, Torpedo, *Phil. Trans. R. S.*, 1887.

Marchand, Contraction wave, *Pflüger's Arch.* vol. xvii., 1878.
Hermann, Diphasic var. of human muscle, *ibid.*, vol. xvi., 1878.
—— Secretion currents, *ibid.*, vol. xvii., 1878.
Gotch, Malapterurus, *J. of Physiol.*, vol. vii., 1886.
—— Torpedo currents, *Phil. Trans. R. S.*, 1887–8.
Sanderson and Gotch, Skate, *J. of Physiol.*, vols. ix. x., 1888–9.
Bayliss and Bradford, Salivary gland currents, *Proc. R. S.*, 1886.
—— Skin currents, *J. of Physiol.*, vol. vii., 1886.
Waller, Electromotive changes of human heart, *J. of Physiol.*, vol. viii., 1887; *Phil. Trans. R. S.* (*Bibl.*), 1889.
Caton, Brain-currents, *Brit. Med. Journal*, 1875; *Trans. Int. Med. Congress*, 1887.
Setschenow, Bulb-currents, *Pflüger's Archiv*, vol. xxvii., 1882.
Gotch and Horsley, Cord-currents, *Phil. Trans. R. S.* (*Croonian Lecture*), 1891.
Tarchanoff, Skin-currents, *Pflüger's Archiv*, vol. xlvi., 1890.
Beck, Brain-currents, *Centralbl. f. Physiol.*, 1890.
v. Fleischl, Brain-currents, *ibid.*, 1890.
Holmgren, Retinal currents, *Cbt. f. med. Wiss.*, 1865; *Unters. Heidelberg*, 1873.
Dewar and McKendrick, Retinal currents, *Trans. R. S. Edinb.*, 1873.
Kühne and Steiner, Retinal currents, *Unters. phys. Inst. Heidelberg*, vol. iii., 1880.
Kühne, Secondary contraction, *Zeitsch. f. Biol.*, vols. xxiv.–vi., 1886–7.

XII. AND XIII. EYE, EAR, &c.

Young, Colour theory, *Natural Philosophy*, London, 1807.
Helmholtz, Colour theories, &c., *Müller's Archiv*, 1852; *Phys. Optik*, 1867.
—— Accommodation, *Monatsber. der Berlin. Akad.*, 1853.
Maxwell, Compound colours, *Phil. Trans. R. S.*, 1860.
Hering, Zur Lehre vom Lichtsinne, *Wien*, 1878.
—— Colour mixtures, *Pflüger's Arch.*, vols. xxxix.–xlvii., 1886–90.
v. Kries, Vision, Colour, *Du Bois-Reymond's Arch.*, 1878, 1882.
Einthoven, Red and blue distance, *Arch. Néerlandaises*, vol. xx., 1886.
König and Dieterici, Colour curves, *Sitzungsberichte*, Berlin, 1886.
Hillebrand, Colour luminosity, *Sitzungsberichte Wien*, 1889.
Abney, Colour measurement and mixture, London, 1891.
Petit, Sympathetic and iris, *Mém. d. l'Acad. des Sc.*, 1727.
Biffi, Sympathetic and iris (section and exc.), *Diss. inaug. Par. Omod. Ann.*, vol. xxii. p. 630, 1846.
Budge and Waller, Cilio-spinal region, *Comptes Rendus de l'Acad. d. Sc.*, 1851.
Budge, Bewegungen d. Iris, *Braunschweig*, 1855.
Schiff, Cilio-spinal region, &c., *Untersuchungen z. Physiol. d. Nerven-Syst.*, Frankfurt, 1855.
Salkowski, Cilio-spinal region, *Zeitsch. f. rat. Med.*, 1867.
Chauveau, Cilio-spinal region, *J. de la Phys.*, 1861.
Guillebeau and Luchsinger, Cilio-spinal region, *Pflüger's Arch.*, vol. xxviii., 1882.
Tuwin, Sup. cerv. gang., *ibid.*, vol. xxiv., 1881.
Waller, Trophic action of retina, *Proc. R. S.*, 1856.
v. Gudden, Optic chiasma, *V. Graefe's Arch. f. Ophthalmol.*, vols. xx. xxi. xxv., 1874–9; *Gesammelte Abhandlungen*, Wiesbaden, 1889.
Michel, Optic chiasma (Bibl.), *Kölliker's Zeitschrift*, Wiesbaden, 1887.
Grünhagen and Samkovy, Inhib. stim. of iris, *Pflüger's Arch.*, vol. x., 1875.
F. Franc, Irido-dilatator nerves, *Travaux du Lab. de Marey*, 1878–9.
Grünhagen, Movements of iris, *Pflüger's Arch.*, vols. iii. x., 1870, 1875.
Gaskell, Structure of irido-dilatator nerves, *Proc. Physiol. Soc.*, 1885.

Bellarminoff, Photochoreograph, *Pflüger's Arch.*, vol. xxxvii., 1886.

Schipiloff, Frog's pupil, *Pflüger's Arch.*, vol. xxxviii., 1890.

Steinach, Crossed reflex of iris, *ibid.*, vol. xlvii., 1890.

Brücke, Chameleon skin, *Wiener Sitzungsber.*, 1851.

Lister, Pigment of frog's skin, *Phil. Trans. R. S.*, 1858.

Boll, Retinal purple, *Du Bois-Reymond's Arch.*, 1877, 1881.

Kühne, Retinal pigments, Optograms, *Untersuch. d. phys. Inst. z. Heidelberg*, vol. i., 1877; *J. of Physiol.*, vol. i., 1878.

Engelmann, Retinal pigment and cones, *Pflüger's Archiv*, vol. xxxv., 1885.

Corti, Cochlea, *Zeitsch. f. wiss. Zool.*, 1851.

Helmholtz, Tonempfindungen, *Braunschweig*, 1870.

König, Beat tones, *Ann. de Physik*, vol. xlvii., 1876.

—— Quelques expériences d'acoustique, *Paris*, 1882.

Exner, Two sounds, *Pflüger's Archiv*, vol. xi., 1875.

v. Hensen, Hearing, *Hermann's Physiologie*, vol. iii., 1879.

Moos and Steinbrugge, Local aff. of cochlea, *Zeitsch. f. Ohrenheilk.*, vol. x., 1880.

Baginsky, Local destruction of cochlea, *Sitzungsber. Berlin*, 1883.

Hermann, Resonation theory, *Pflüger's Archiv*, vol. xlix., 1891.

Goltz, Semicircular canals, *ibid.*, vol. iii., 1870.

Mach, Semicircular canals, *Wiener Sitzungsber.*, 1873; *Lehre von den Bewegungsempfindungen*, Leipsig, 1875.

Cyon, Semicircular canals, *Pflüger's Arch.*, vol. viii., 1874.

Crum Brown, Semicircular canals, *J. of Anat. and Phys.*, 1875.

Spamer, Semicircular canals (Bibl.), *Pflüger's Arch.*, vol. xxi., 1880.

Sewall, Semicircular canals, *J. of Physiol.*, vol. iv., 1883–4.

Breuer, Semicircular Canals, *ibid.*, 1889.

Ewald, Semicircular canals, *Centralbl. f. med. Wiss.*, 1890; *Pflüger's Arch.*, vol. xliv., 1889.

Loeb, Forced movements, *Pflüger's Archiv*, vol. l., 1891.

Golgi, Sui nervi dei tendinei, &c., *Torino*, 1880.

A. Goldscheider, Muscular sense (joints), *Du Bois-Reymond's Arch.*, 1889.

Bastian and others, Discussion on the muscular sense, *Brain*, 1887.

Blix, Hot and cold areæ, *Zeitsch. f. Biologie*, 1884.

A. Goldscheider, Hot and cold areæ, *Du Bois-Reymond's Archiv*, 1885.

Herzen, Hot and cold nerves, *Pflüger's Archiv*, vol. xxxviii., 1886.

XIV. AND XV. SPINAL CORD AND BRAIN

Descartes, Reflex action (about 1640), *Œuvres complètes* (*Cousin*), Paris, 1824.

—— Les Passions de l'Ame, *Paris*, 1649.

Charles Bell, Nerve roots, Respiratory nerves, *An Idea of a New Anatomy of the Brain*, 1811, republished in *An Exposition of the Natural System of Nerves*, London, 1824; *The Nervous System of the Human Body*, London, 1830.

Magendie, Sensory and motor roots, *J. de Physiol. Exp.*, 1822.

J. Müller, Nerve roots of frog, *Froriep's Notizen d. Natur- u. Heilkunde*, 1831.

Longet, Système nerveux, *Paris*, 1842.

Bernard, Système Nerveux, *Paris*, 1858.

Marshall Hall, Reflex action, *Phil. Trans.*, 1833; *Memoirs on the Nervous System*, London, 1837.

Waller, Trophic influence of nerve-cells, *Nouvelle Méthode, &c.*, Bonn, 1851.

Türck, Cord degeneration, *Sitzungsberichte*, 1851; Wien, 1853.

Stilling, Unters. ü. d. Functionen des Rückenmarks, *Leipsig*, 1842.

van Deen, Spinal cord, *Moleschott's Unters.*, vols. vi. vii., 1860.

van Deen, Traités et Découv. sur la Phys. de la Moelle Epinière, *Leiden*, 1841.
Chauveau, Excitability of cord, *J. de la Physiologie*, 1861.
Bernard, Recurrent sensibility in nerve-roots, *Leçons sur le Système Nerveux*, 1858.
Arloing and Tripier, Recurrent sensibility in periph. nerves, *Arch. de Phys.*, 1876.
Wundt, Unters. z. Mechanic. d. Nerven u. d. Nervencentren, *Erlangen u. Stuttgart*, 1871–6.
Guttmann, Inexcitability of brain and cord, *Du Bois-Reymond's Arch.*, 1866.
Engelken (Fick), Excit. of cord, *ibid.*, 1867.
S. Mayer, Inexcitability of cord, *Pflüger's Arch.*, vol. i., 1868.
Luchsinger, Exc. of cord, *ibid.*, vol. xxii., 1880.
Fick, Excitability of ant. columns, *ibid.*, vol. ii., 1869.
Huizinga, Inexcitability of ant. col., *ibid.*, vol. iii., 1870.
Flechsig, Development and spinal columns, *Leitungsbahnen in Gehirn u. Rückenmark*, *Leipsig*, 1876; *Plan des menschlichen Gehirns*, 1883.
Lewaschew (Breslau), Double decussation, *Pflüger's Archiv.*, vol. xxxvi., 1885.
Homèn, Moelle épinière, *Helsinfors*, 1885.
Tooth, Secondary Degenerations of Cord, *London*, 1889.
Mott, Hemisection of cord, *Phil. Trans. R.S.*, 1891.
Golgi, Sulla fina anatomia degli organi centrali del sistema nervoso, *Milano*, 1886.
Rumpf, Dissol. of cord, *Pflüger's Archiv*, vol. xxvi., 1881.
Bechterew, Equilibration, Spinal paths, *ibid.*, vol. xxix. p. 257, 1882.
Brown-Séquard, Brain and cord transmission, *J. de la Physiologie*, 1863; *Lancet*, 1858.
—— Exper. and Clin. Researches, *Richmond*, 1855.
—— Rech. et Exp. sur la Phys. de la Moelle Epinière, *Paris*, 1856.
Schiff, Varia, *Lehrbuch. d. Physiol.*, 1858–9.
Vulpian, Système Nerveux, *Paris*, 1866.
Pflüger, Sensor. Funct. d. Rückenmarks, *Berlin*, 1853.
—— Spinal cord discrimination, *Pflüger's Arch.*, vol. xv., 1877.
Goltz, Beiträge z. Nervencentren des Frosches, *Berlin*, 1869.
Osawa and Tiegel, Snakes, *Pflüger's Arch.*, vol. xvi., 1878.
Setschenow, Stud. ü. d. Hemmungsmech. d. Rückenmarkes, *Berlin*, 1863.
Lewisson, Inhibition, *Du Bois-Reymond's Arch.*, 1869.
Exner, Reflex winking time, *Pflüger's Arch.*, vol. viii., 1874.
Waller, Tendon-reflex (Bibliogr.), *J. of Physiology*, 1890.
Brondgeest, Reflex tonus, *Arch. f. die Holländ. Beitr. zur Natur- u. Heilk.*, 1860.
Dittmar, Spinal cord paths, *Ludwig's Arbeiten*, 1870, 1873.
Miescher, Spinal cord paths, *ibid.*, 1870.
Nawrocki, Spinal cord paths, *ibid.*, 1871.
Woroschiloff, Spinal cord paths, *ibid.*, 1874.
Gaskell, Cranial nerves, *J. of Physiology*, vol. x., 1889.
Ferrier and Yeo, Brachial and sacral plexus, *Proc. R. S.*, 1881.
Bidder and Volckmann, Die Selbständigkeit des sympathischen Nervensystems, *Leipsig*, 1842.
Kölliker, Die Selbständigkeit und Abhängigkeit des sympathischen Nervensystems, *Zürich*, 1844.
Reissner, Large and small nerve-fibres, *Du Bois-Reymond's Archiv*, 1862
Birge, Number of spinal nerve-cells, *ibid.*, suppl. 1882.
Gaule, Number of spinal nerve-fibres, *Abh. d. Sächs. Ges. d. Wissensch.*, 1889
Gaskell, Large and small nerve-fibres, *Journ. of Physiol.*, vol. vii., 1886.
Gall and Spurzheim, Recherches sur le Système Nerveux, Cerveau, *Paris*, 1809.
Bouillaud, Localisation, *Arch. de Médecine*, 1825.

Dax, Localisation, *J. de Physiol. Exp.*, 1830.

Flourens, Cerebellum, &c., *Système Nerveux*, Paris, 1842.

Hughlings Jackson, Localisation, Dissolution, *Clinical and Pathological Researches on the Nervous System*, 1861; *British Medical Journal*, 1890; *Lancet*, 1873.

Charcot, Leçons sur les Maladies du Système Nerveux, *Paris*, 1872–3.

Fritsch and Hitzig, Ueber die elektrische Erregbarkeit des Grosshirns, *Du Bois-Reymond's Arch.*, p. 300, 1870.

Ferrier, Exp. res. in cerebr. physiol. and pathol., *West Riding Lunatic Asylum Reports*, 1873.

Nothnagel, Mech. exc. of cortex, *Virchow's Arch.*, 1873.

—— Nervencentren d. Frosches, *Berlin*, 1869.

Goltz, Dog's brain, *Pflüger's Archiv*, vols. xiii.–xxxiv., 1876–84.

B. Sanderson, Subcortical excitation, *Proc. R. S.*, 1874; *Centralbl. f. med. Wiss.*, 1874.

Dupuy, Critical review of 'localisation,' *London Med. Times and Gazette*, 1877.

Luciani and Tamburini, Psycho-motor cortex, *Rivista Speriment. di Freniatria*, 1878–9.

—— Pyscho-sensory cortex, *ibid.*, 1879.

Munk, Ueber die Functionen der Grosshirnrinde, *Berlin*, 1881; *Du Bois-Reymond's Arch.*, 1878.

Broca, Olfactory lobe, *Revue d'Anthropologie*, 1878–9.

Exner, Localisation der Functionen in der Grosshirnrinde des Menschen, 1881.

Bubnoff and Heidenhain, Ueber Erregungs- und Hemmungsvorgänge innerhalb der motorischen Hirncentren, *Pflüger's Archiv*, vol. xxvi., 1881.

Danillo, Absinthe, *Arch. de Physiol.*, 1882.

Sciamanna, Cort. exc. on man, *Arch. de Psychiatria*, 1882.

Ferrier and Yeo, Localisation, *Phil. Trans. R. S.*, 1884.

Luciani and Seppilli, Le localizzazioni funzionali del cervello, *Napoli*, 1885.

Luciani, Mech. exc. of cortex, *Arch. Ital. de Biol.*, vol. iv., 1884.

Christiani, Zur Physiologie des Gehirns, *Berlin*, 1885.

Exner and Paneth, Circumvallation of motor centres, *Pflüger's Arch.*, vol. xliv., 1889.

Ferrier, *Functions of the Brain*, 1st ed. 1876, 2nd ed. 1886.

F. Franc, Fonctions du Cerveau, *Paris*, 1887.

Schäfer and Horsley, Localisation, *Phil. Trans. R. S.*, 1888.

Beevor and Horsley, Localisation, *ibid.*, 1888, 1890.

Ferrier, The Croonian lectures on cerebral localisation, *British Medical Journal*, 1890.

Loeb, Goltz, Zuntz, Cortical areæ, Visual area, *Pflüger's Archiv*, vol. xxxiv., 1884; vol. xxxix., 1886.

Gerber (Hermann), An. and kath. exc. of brain, *ibid.*, vol. xxxix., 1886.

Steiner, Frog Brain, *Braunschweig*, 1885.

—— Fish Brain, *Braunschweig*, 1888.

Schrader, Brainless frogs, *Pflüger's Arch.*, vol. xli., 1887.

Durham, Cerebral circulation, *Guy's Hospital Reports*, 1860.

Mosso, Sulla circulazione del sangue nel cervello dell' uomo, *Roma*, 1880.

Roy and Sherrington, Circulation in brain, *J. of Phys.*, vol. xi., 1890.

Liebreich, Protagon, *Annalen d. Chem. and Phys.*, 1865.

Gamgee, Protagon, *J. of Phys.*, 1879.

Ewald and Kühne, Neuro-keratin, *Verh. d. naturhist. Vereins. z. Heidelberg*, 1877; *Zeitsch. f. Biologie*, vol. xxvi., 1890.

Gad and Heymans, Composition of myelin, *Du Bois-Reymond's Arch.*, 1890.
Weber, Sensation ratio, *Wagner's Handwörterb. d. Physiol.*, 1842–53.
Fechner, Elemente der Psychophysic, 1860. 2nd edit. 1889.
Exner, Reaction time, *Pflüger's Arch.*, vols. vii. xv., 1873.
Vintschgau, Reaction time, *ibid.*, vols. vii. x. xiv. xvi., 1875, 1877, 1878.
Kries and Auerbach, Reaction time, *Du Bois-Reymond's Arch.*, 1877.
Münsterberg, Beiträge zur exper. Psychol., 1889–90.
—— Die Willenshandlung, 1888.
Braid, Neurypnology, Nervous Sleep, Animal Magnetism, *London*, 1843.
Binet and Féré, Le Magnétisme Animal, *Paris*, 1887.
Hack Tuke, Influence of Mind upon Body, &c., *London*, 1872; 3rd ed. 1889.
Heidenhain, Der sogenannte thierische Magnetismus, *Leipsig*, 1880.
Preyer, Hypnotismus, *Berlin*, 1881.
Richer, Hystéro-épilepsie, *Paris*, 1881; 2nd ed. 1885.
Bernheim, De la Suggestion, &c., *Paris*, 1888.
Page, Railway injuries, *London*, 1891.

EMBRYOLOGY

Preyer, Physiologie de l'Embryon (literature to date), *Leipsig*, 1885.
Liebermann, Embryo chemistry, *Pflüger's Arch.*, vol. xliii., 1888.
Cohnstein and Zunts, *ibid.*, vol. xlii., 1888.
Hermann and v. Gendre, E.M.F. of embryo chick, *Pflüger's Archiv*, vol. xxxv., 1885.
Paterson, Mesoblastic origin of sympathetic, *Phil. Trans. R. S.*, 1890.
His, Histogenesis of nerve elements, *Arch. f. Anat.* (suppl.), 1890.
Schäfer, Quain's Anatomy (literature to date), 10th edit., 1891.

INDEX

Abducens, or sixth, nerve, 499
Absorption of food, 158
— in intestinal tract, 211–3
Accelerator fibres to heart, 98, 105
— — in vagus, 103
Accommodation (fig. 208), 415
— phosphene, 440
— power at different ages (fig. 209), 416
Acetic acid, 571, 573
Acetone, 571
Achroodextrin, 168
Acid albumin, 185
— — tests, 192, 193
Acids, effect on heart, 96
Acini of glands, 170–4
Action currents, 369
Aeby, on contraction of muscle, 327
Aerotonometer, 136
Afferent fibres, proof of their existence, 351
— nerves, 344–9, (fig. 107), 292
— — classification of, 347–8
— — in respiration, 147
After-images, 447–8
— -effects, electrotonic, 368, 373
Air, saturation of expired, 246
Air-pressure on lungs and heart, 142
— supply, 121, 124, 129
Albumin in urine, 242
Albumins, tests for, 192, 193
Albuminuria, 242
Albumose, 185
— tests, 192, 193
— nature of, 194
— summary, 195
Alizarin blue, action of tissues on, 138
Alkali albumin, tests for, 192, 193
Alkalies, effect on heart, 96
Allantoin, 575
Allantois, 560–1
Alveolar air, tension of, 136
Alveoli of lung, 118
Amido-acetic acid, 573
Amido-caproic acid, 574
Ammonia formula, 571
Amnion, 561
Amœba, 290
Amœboid movements of corpuscles, 23
Ampère, 305
Amylolytic ferment, 204
Anabolic or constructive change, 1, 105, 567
— effect of vagus, 105
Anæmia, 20
Anæsthesia, 476, 505
Anelectrotonus, 366–8, 371
Animal fat, 572
— heat, 275–89
Anisotropic substance (fig. 128), 319
Anode, 302, 361
— diminution of excitability at, 370
Anodic break contractions, 364–5
Anti-albumose, 186
Aorta, pressure in, 142
Aphasia, 529–32
Aphonia, 153
Apnœa, 127
— effect on sugar production, 220
Apomorphine, 166
Aqueous humour (fig. 200), 409
Argutinski, on excretion of urea, 265
Argyll-Robertson pupil, 434
Aromatic bodies, 240, 576
Aronsohn and **Sachs**, on punctures of brain, 283
Arterial blood, 18–20
— — pulmonary, 121
— pressure, effect of respiration on, 140–1, (fig. 59) 140
Arteries of the brain, 512–3
Arterioles, resistance of, 59
Artificial respiration, 144
Ashdown, on sugar reaction in urine, 220
Asphyxia, 125, (fig. 57) 126
Assimilation, 1, 248, 268
— visual, 407, 546
Astigmatism, 422–3
Atelectasis, 118
Atmospheric air cp. with expired air, 121, 124
Atrophy, 268
Atropin, arrests secretion, 177, 180
— action on pupil, 435
Attention, 550
Auditory, or eighth nerve, 499
— centre, 524